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NOV 28 7:

SEARCH REQUEST FORM

Scientific and Technical Information Center

(STIC)

Requester's Full Name: Gary Nickol Examiner #: 77581 Date: 11/28/01

Art Unit: 1642 Phone Number 305-7143 Serial Number: 09/308223

Mail Box and Bldg/Room Location: 3E12, 8D09 Results Format Preferred (circle): (PAPER) DISK E-MAIL

If more than one search is submitted, please prioritize searches in order of need. 1 2 3

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Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc, if known. Please attach a copy of the cover sheet, pertinent claims, and abstract.

Title of Invention: Attached

Inventors (please provide full names): Attached

Earliest Priority Filing Date: 11/19/96

***For Sequence Searches Only* Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.** (see attached)

I am primarily concerned with claims 13 + 27. Note the broad terminology of "lyophilizate" + "surfactant".

A Lyophilizate = freeze dried compositions.

Surfactants include "Tween", "detergents", polysorbates - see claim 24.

Also "essentially free" is a broad term and doesn't mean the composition cannot have ANY polyethylene glycols.

Thanks,

GARY

Point of Contact:
Beverly Sheere
Technical Info. Specialist
CM1 [redacted] Tel: 308-4242
1E05

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STAFF USE ONLY	Type of Search	Vendors and cost where applicable
Searcher: B. Jones	NA Sequence (#)	STN ✓
Searcher Phone #:	AA Sequence (#)	Dialog
Searcher Location:	Structure (#)	Questel/Orbit
Date Searcher Picked Up:	Bibliographic	Dr.Link
Date Completed: 12-04-01	Litigation	Lexis/Nexis
Searcher Prep & Review Time: 12	Fulltext	Sequence Systems
Clerical Prep Time:	Patent Family	WWW/Internet
Online Time: 32	Other	Other (specify)

PTO-1590 (8-01)

above-mentioned **detergents** was simpler and less time consuming than by the .beta.-naphthol method.

IT **9005-65-6**
RL: BIOL (Biological study)
(in antigen purification)

L11 ANSWER 37 OF 37 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1962:63281 CAPLUS
DOCUMENT NUMBER: 56:63281
ORIGINAL REFERENCE NO.: 56:12161c-g
TITLE: Chemical nature of mouse histocompatibility antigens
AUTHOR(S): Davies, D. A. L.
CORPORATE SOURCE: Microbiol. Research Estab., Salisbury, UK
SOURCE: Nature (1962), 193, 34-6
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable

AB Readily dispersible but essentially insol. prepns. of mouse H2 histocompatibility antigen (I) can be prepd. from ascitic fluid. I was not pptd. by (NH4)2SO4, was irreversibly adsorbed on substituted ionexchanger cellulose, was labile to heat, acid, alkali, ultrasonication, and **freeze-drying**. An insol. fraction contg. all I formed when C3H mouse ascitic fluid (BP8 tumor) was dialyzed or dild. with more than 1 vol. H2O. All I activity was sedimented in 90 min. at 80,000 g. Sedimentation 4 times from saline and 2 times from H2O removed all serum proteins. Results of differential centrifugation at intermediate speeds suggested gross polydispersity of particle size. The most active fractions were centrifuged to equil. at 100,000 g in a **sucrose** d. gradient. All activity was in the T4 and T5 sedimentation bands, both giving specific inhibition, but only the T5 band (II) was capable of inducing agglutinating H2 **antibody** formation when injected into mice of appropriate strains. About 120 mg. of II was obtained from 1000 mice; the compn. was 10% N, 1.0% P, 0.5% S, 60% protein, 3.5% carbohydrate, 35% lipid, 1% hexosamine, and 0.3% sialic acid, and it gave a milky suspension in H2O but flocculated in saline. In the ultracentrifuge II was polydisperse and sedimented rapidly. II was homogeneous by electrophoresis, d.-gradient centrifugation, and immunological techniques. The smallest entity with I activity may still not have been prepd. Materials from different inbred mouse strains may have differences in lipid compn. Prepns. from C3H, C57Bl, and BALB/c mice carry specificities expected from the known distribution of H2 alleles. On purification of antigen the lipid content increased with increasing activity. The protein component had a specificity of its own, other than I, which was not exposed on cell surfaces, whereas I specificity was exposed. I specificity was lost in **freeze-drying**, treatment with Na dodecyl sulfate, deoxycholate, **Tween** 20, lysolecithin, and periodate.

(FILE 'MEDLINE, BIOSIS, EMBASE, WPIDS, CONFSCI, SCISEARCH, JICST-EPLUS, JAPIO' ENTERED AT 12:35:06 ON 04 DEC 2001)
L12 38 SEA ABB=ON PLU=ON L6 AND (L10 OR MONOSACCHARIDE OR TRISACCHARIDE OR DISACCHARIDE OR SACCHARIDE)
L13 29 DUP REM L12 (9 DUPLICATES REMOVED)

L13 ANSWER 1 OF 29 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
ACCESSION NUMBER: 2001-549774 [61] WPIDS

DOC. NO. CPI: C2001-163566
TITLE: Liquid biodegradable block copolymer composition, useful as a drug delivery system for e.g. growth hormones, antibacterial agents, anticancer or antiinflammatory agents.
DERWENT CLASS: A96 B05 B07
INVENTOR(S): CHOI, I; SEO, M
PATENT ASSIGNEE(S): (SAMY-N) SAMYANG CORP
COUNTRY COUNT: 93
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2001045742	A1	20010628	(200161)*	EN	37

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW

AU 2001025550 A 20010703 (200164)

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2001045742	A1	WO 2000-KR1508	20001221
AU 2001025550	A	AU 2001-25550	20001221

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2001025550	A Based on	WO 200145742

PRIORITY APPLN. INFO: KR 1999-60349 19991222
AN 2001-549774 [61] WPIDS
AB WO 200145742 A UPAB: 20011024
NOVELTY - A liquid polymeric composition capable of forming a physiologically active substance-containing implant in a living body is new.

DETAILED DESCRIPTION - A liquid polymeric composition capable of forming a physiologically active substance-containing implant in a living body comprises a water-soluble liquid polyethylene glycol derivative, a block copolymer which is insoluble in water but soluble in the polyethylene glycol derivative and an active substance.

INDEPENDENT CLAIMS are included for:
(1) an implant formed from the composition; and
(2) processes for preparing the composition.

USE - The composition is useful for forming active substance containing implants for drug delivery when injected into a body.
Dwg.0/1

L13 ANSWER 2 OF 29 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
ACCESSION NUMBER: 2001-407957 [43] WPIDS
DOC. NO. NON-CPI: N2001-301872

DOC. NO. CPI: C2001-123491
TITLE: Oral transmucosal solid dosage form drug delivery formulation comprises pharmaceutical agent absorbable into oral mucosal tissue and present in solid solution with dissolution agent.
DERWENT CLASS: A96 B05 P32
INVENTOR(S): CROFT, J; ZHANG, H
PATENT ASSIGNEE(S): (ANES-N) ANESTA CORP
COUNTRY COUNT: 94
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2001030288	A1	20010503	(200143)*	EN	32
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TZ UG ZW					
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG UZ VN YU ZA ZW					
US 6264981	B1	20010724	(200146)		
AU 2001010797	A	20010508	(200149)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2001030288	A1	WO 2000-US28113	20001012
US 6264981	B1	US 1999-428071	19991027
AU 2001010797	A	AU 2001-10797	20001012

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 2001010797	A	Based on	WO 200130288

PRIORITY APPLN. INFO: US 1999-428071 19991027
AN 2001-407957 [43] WPIDS
AB WO 200130288 A UPAB: 20010801
NOVELTY - An oral transmucosal solid dosage form drug delivery formulation comprises a pharmaceutical agent capable of being absorbed into oral mucosal tissue, and a dissolution agent. The pharmaceutical agent is in solid solution with the dissolution agent. The dissolution agent has a rate in the solvents found in the oral cavity greater than that of the pharmaceutical agent.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for oral transmucosal delivery of a pharmaceutical agent by providing a drug formulation having a solid pharmaceutical agent in solid solution with a dissolution agent, administering the formulation into a patient's oral cavity, and delivering the pharmaceutical agent by absorption through a patient's mucosal tissue.

USE - The invention is used for oral transmucosal delivery of a pharmaceutically active substance.

ADVANTAGE - The invention produces faster dissolution rates and, accordingly, higher absorption rates of the pharmaceutically

active substance. It can afford better solubility in saliva and mucosal absorption without comprising stability of the solid dosage during storage.
Dwg.0/3

L13 ANSWER 3 OF 29 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
ACCESSION NUMBER: 2001-244222 [25] WPIDS
DOC. NO. CPI: C2001-073233
TITLE: Pharmaceutical system for improved absorption of hydrophilic agent includes hydrophilic **surfactant** and is free of triglycerides.
DERWENT CLASS: A96 B05 B07 D16
INVENTOR(S): CHEN, F; FIKSTAD, D T; PATEL, M V
PATENT ASSIGNEE(S): (LIPO-N) LIPOCINE INC; (CHEN-I) CHEN F; (FIKS-I) FIKSTAD D T; (PATE-I) PATEL M V
COUNTRY COUNT: 94
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2001012155	A1	20010222	(200125)*	EN	112
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TZ UG ZW					
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG UZ VN YU ZA ZW					
AU 2000060838	A	20010313	(200134)		
US 2001024658	A1	20010927	(200159)		

APPLICATION DETAILS:

PATENT NO	KIND		APPLICATION	DATE
WO 2001012155	A1		WO 2000-US18807	20000710
AU 2000060838	A		AU 2000-60838	20000710
US 2001024658	A1	CIP of	US 1999-375636	19990817
			US 2000-751968	20001229

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 2000060838	A	Based on	WO 200112155

PRIORITY APPLN. INFO: US 1999-375636 19990817
AN 2001-244222 [25] WPIDS
AB WO 200112155 A UPAB: 20010508
NOVELTY - Pharmaceutical system comprises:
(1) a dosage form of an absorption enhancing composition comprising at least 2 **surfactants**, and
(2) a hydrophilic therapeutic agent.
The system is free of triglycerides
DETAILED DESCRIPTION - An INDEPENDENT CLAIM is included for the above absorption enhancing composition.
USE - Used for controlling the rate and/or extent of bioabsorption of the therapeutic agent.

In a relative absorption study, a sample preconcentrate solution comprising (in g): 0.30 Cremophor RH40, 0.20 Arlacel 186, 0.18 sodium taurocholate and 0.32 propylene glycol was diluted with standard hypotonic PBS pH 7.4 buffer and spiked with 0.1 mM cold acyclovir, then 0.5 mu l tritiated acyclovir (specific activity 18.9 Ci/mmol). The obtained aqueous isotonic dispersion was perfused through rat intestinal segments and the appearance of the acyclovir in the mesenteric blood was monitored along with disappearance on the luminal side. Results showed that the absorption of acyclovir relative to a plain buffer was 704%.

ADVANTAGE - Bioabsorption of the therapeutic agent is improved

Dwg.0/0

L13 ANSWER 4 OF 29 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD

ACCESSION NUMBER: 2001-168427 [17] WPIDS
DOC. NO. NON-CPI: N2001-121465
DOC. NO. CPI: C2001-050270
TITLE: New **lyophilized**, rigid, **surfactant** free reagent spheres, for use in diagnostic detection of antigens in whole cell samples.
DERWENT CLASS: B04 D16 S03
INVENTOR(S): GOERTZ, S; HEMMES, P
PATENT ASSIGNEE(S): (SPEC-N) SPECTRAL DIAGNOSTICS INC
COUNTRY COUNT: 93
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2001004633	A2	20010118	(200117)*	EN	34

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG UZ VN YU ZA ZW

AU 2000060088 A 20010130 (200127)

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2001004633	A2	WO 2000-IB967	20000714
AU 2000060088	A	AU 2000-60088	20000714

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 2000060088	A	Based on	WO 200104633

PRIORITY APPLN. INFO: US 2000-616018 20000713; US 1999-353191 19990714

AN 2001-168427 [17] WPIDS

AB WO 200104633 A UPAB: 20010328
NOVELTY - **Lyophilized**, rigid reagent spheres (I), essentially free of **surfactant**, comprise a reagent useful

to detect an analyte in a given sample.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:
(1) producing (I); and
(2) bioassay using (I).
USE - (I) are particularly used to perform **antibody** /antigen reactions, e.g. to detect cardiac or bacterial antigens, cytokines, drugs of abuse (or their metabolites), typically for diagnosis of sepsis and myocardial infarction.
ADVANTAGE - Since they are free of lytic **surfactants**, (I) can be used where the test system includes intact cells, e.g. whole blood or its cell-containing fractions. (I) retain all the advantages of known reagent spheres, i.e. rapid dissolution, ease of handling, adequate mechanical stability and uniform distribution of reagents.
Dwg.0/0

L13 ANSWER 5 OF 29 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
ACCESSION NUMBER: 2001-496382 [54] WPIDS
CROSS REFERENCE: 1997-145374 [13]; 1997-145380 [13]; 2001-496010 [51]
DOC. NO. CPI: C2001-148984
TITLE: Reconstituted protein formulation for treating chronic medical condition in mammals comprises **lyophilized** mixture of a protein/**antibody** and a lyoprotectant.
DERWENT CLASS: B04 D16
INVENTOR(S): ANDYA, J; CLELAND, J L; HSU, C C; LAM, X M; OVERCASHIER, D E; SHIRE, S J; WU, S S; YANG, J Y
PATENT ASSIGNEE(S): (GETH) GENENTECH INC
COUNTRY COUNT: 1
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
US 2001014326	A1	20010816	(200154)*		30

APPLICATION DETAILS:

PATENT NO	KIND		APPLICATION	DATE
US 2001014326	A1	Cont of	US 1995-508014	19950727
		Div ex	US 1996-615369	19960314
		Provisional	US 1996-29182P	19960729
			US 2001-809511	20010314

PRIORITY APPLN. INFO: US 1996-29182P 19960729; US 1995-508014 19950727; US 1996-615369 19960314; US 2001-809511 20010314
AN 2001-496382 [54] WPIDS
CR 1997-145374 [13]; 1997-145380 [13]; 2001-496010 [51]
AB US2001014326 A UPAB: 20010924
NOVELTY - An isotonic reconstituted formulation (I) comprising a protein/**antibody** (at least 50 mg/ml) and a diluent is prepared from a **lyophilized** mixture of a protein/**antibody** and a lyoprotectant. The protein/**antibody** concentration in the formulation is 2 - 40 times greater than in the

mixture before **lyophilization**.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) preparation of (I);

(2) an article comprising a container holding the **lyophilized** mixture of the protein and the lyporotectant and instructions for reconstituting the **lyophilized** mixture with the diluent to the protein concentration of at least 50 mg/ml.

USE - For treating mammals (claimed) having chronic medical conditions.

ADVANTAGE - The formulation is sterile, **lyophilized** and stable at 30 deg. C for at least 6 months or 1 year. The formulation is stable at 2-8 deg. C for at least 30 days. The formulation retains its physical and chemical stability and integrity on **lyophilization** and storage. The multi-use formulation facilitates ease of use for the patient, reduces waste by allowing complete use of vial contents and results in significant cost saving for the manufacturer since several doses are packaged in a single vial (lower filling and shipping costs).

Dwg.0/19

L13 ANSWER 6 OF 29 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD

ACCESSION NUMBER: 2001-496010 [54] WPIDS

CROSS REFERENCE: 1997-145374 [13]; 1997-145380 [13]; 2001-496382 [54]

DOC. NO. CPI: C2001-148870

TITLE: Stable isotonic reconstituted formulation useful for treating allergy, asthma and cancer, comprises specified amount of **antibody** and diluent, and is prepared from **lyophilized** mixture of **antibody** and lyoprotectant.

DERWENT CLASS: B04 D16

INVENTOR(S): ANDYA, J; CLELAND, J L; HSU, C C; LAM, X M; OVERCASHIER, D E; SHIRE, S J; WU, S S; YANG, J Y

PATENT ASSIGNEE(S): (GETH) GENENTECH INC

COUNTRY COUNT: 1

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
US 6267958	B1	20010731	(200154)*		29

APPLICATION DETAILS:

PATENT NO	KIND		APPLICATION	DATE
US 6267958	B1		US 1996-615369	19960314
		Provisional	US 1996-29182P	19960727

PRIORITY APPLN. INFO: US 1996-29182P 19960727; US 1996-615369 19960314

AN 2001-496010 [54] WPIDS

CR 1997-145374 [13]; 1997-145380 [13]; 2001-496382 [54]

AB US 6267958 B UPAB: 20010924

NOVELTY - A stable isotonic reconstituted formulation (I) comprises 50-400 mg/mL of an **antibody** (Ab) and a diluent, prepared from a **lyophilized** mixture of Ab and a lyoprotectant (L)

which prevents or reduces chemical or physical instability of Ab upon **lyophilization** and subsequent storage.

DETAILED DESCRIPTION - A stable isotonic reconstituted formulation (I) comprises 50-400 mg/mL of an **antibody** (Ab) and a diluent, prepared from a **lyophilized** mixture of Ab and a lyoprotectant (L) which prevents or reduces chemical or physical instability of Ab upon **lyophilization** and subsequent storage.

In (I), the molar ratio of (L):Ab is about 100-510 mole (L):1 mole of Ab, and Ab concentration in (I) is 2-40 times greater than Ab concentration in the mixture before **lyophilization**.

INDEPENDENT CLAIMS are also included for the following:

(1) preparation of (I); and

(2) an article of manufacture (II) comprising a container which holds the **lyophilized** mixture of an **antibody** and lyoprotectant which prevents or reduces chemical or physical instability of **antibody** upon **lyophilization** and subsequent storage, where the molar ratio of lyoprotectant: **antibody** is about 100-510 mole lyoprotectant:1 mole of **antibody**, and instructions for reconstituting the **lyophilized** mixture with a diluent to an **antibody** in the reconstituted formulation of about 80-400 mg/ml.

ACTIVITY - Cytostatic; antiallergic; antiasthmatic; antiparasitic.

No supporting biological data is given.

MECHANISM OF ACTION - None given.

No supporting biological data is given.

USE - (I) is useful for treating chronic and acute disorders or diseases such as allergy, parasitic infection, interstitial cystitis, asthma, and cancer of breast, ovary, stomach, endometrium, salivary gland, lung, kidney, colon and/or bladder.

ADVANTAGE - (I) is reconstituted to generate a stable reconstituted formulation having a protein concentration which is significantly higher than the protein concentration in the pre-**lyophilized** formulation. (I) is a multi-use formulation and facilitates ease of use for the patient, reduces waste by allowing complete use of viral contents, and results in a significant cost savings for the manufacturer, since several doses are packaged in a single vial (lower filling and shipping costs).

Dwg.0/19

L13 ANSWER 7 OF 29 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD

ACCESSION NUMBER: 2001-136863 [14] WPIDS

DOC. NO. CPI: C2001-040061

TITLE: Stable aqueous pharmaceutical formulation for treating hemorrhagic shock, thermal injury, stroke, and myocardial infarction, comprises an **antibody** not subjected to prior **lyophilization**.

DERWENT CLASS: B04 D16

INVENTOR(S): LAM, X M; OESWEIN, J Q; ONGPIPATTANAKUL, B; SHAHROKH, Z; WANG, S X; WEISSBURG, R P; WONG, R L

PATENT ASSIGNEE(S): (GETH) GENENTECH INC

COUNTRY COUNT: 1

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG

US 6171586 B1 20010109 (200114)* 56

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
US 6171586	B1 Provisional	US 1997-53087P	19970613
		US 1998-97171	19980612

PRIORITY APPLN. INFO: US 1997-53087P 19970613; US 1998-97171 19980612

AN 2001-136863 [14] WPIDS

AB US 6171586 B UPAB: 20010312

NOVELTY - A stable aqueous pharmaceutical formulation (I), comprising an **antibody** (Ab) not subjected to prior **lyophilization**, an acetate buffer of pH 4.8-5.5, a **surfactant** and a polyol, and lacking sodium chloride, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) an article of manufacture (II) comprising a container containing (I); and

(2) stabilizing Ab in (I), by combining Ab not subjected to prior **lyophilization**, an acetate buffer of pH 4.8-5.5, a **surfactant** and a polyol, without sodium chloride.

ACTIVITY - Hemostatic; vasotropic; cerebroprotective; vulnerary; cardiant; antiinflammatory; antiulcer; antirheumatic; antiarthritic; cytostatic.

MECHANISM OF ACTION - Vaccine.

No biological data is given.

USE - (I) is useful for treating hemorrhagic shock, thermal injury, e.g. resulting from burns, stroke including ischemic and hemorrhagic stroke, myocardial infarction, inflammatory disorders such as adult respiratory distress syndrome (ARDS), hypovolemic shock, ulcerative colitis, rheumatoid arthritis and B-cell lymphomas.

Dwg.0/28

L13 ANSWER 8 OF 29 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.DUPLICATE 1

ACCESSION NUMBER: 2001371848 EMBASE

TITLE: The effects of **Tween** 20 and **sucrose** on the stability of anti-L-selectin during **lyophilization** and reconstitution.

AUTHOR: Jones L.S.; Randolph T.W.; Kohnert U.; Papadimitriou A.; Winter G.; Hagmann M.-L.; Manning M.C.; Carpenter J.F.

CORPORATE SOURCE: J.F. Carpenter, School of Pharmacy, Univ. of Colorado Hlth. Sci. Center, Denver, CO 80262, United States. john.carpenter@uchsc.edu

SOURCE: Journal of Pharmaceutical Sciences, (2001) 90/10 (1466-1477).
Refs: 39
ISSN: 0022-3549 CODEN: JPMSAE

COUNTRY: United States

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 037 Drug Literature Index
039 Pharmacy

LANGUAGE: English
SUMMARY LANGUAGE: English
AB We have chosen an anti-L-selectin **antibody** as a model protein to investigate the effects of **sucrose** and/or **Tween** 20 on protein stability during **lyophilization** and reconstitution. Native anti-L-selectin secondary structure is substantially retained during **lyophilization** in the presence of **sucrose** (1 or 0.125%). However, aggregation of the protein during reconstitution of **lyophilized** protein powders prepared without **sucrose** is not reduced by the presence of **sucrose** in the reconstitution medium. Aggregate formation upon reconstitution is completely inhibited by **freeze drying** the protein with **sucrose** and reconstituting with a 0.1% **Tween** 20 solution. **Tween** 20 (0.1%) also partially inhibits loss of native anti-L-selectin secondary structure during **lyophilization**. However, upon reconstitution the formulations **lyophilized** with **Tween** 20 contain the highest levels of aggregates. The presence of **Tween** in only the reconstitution solution appears to inhibit the transition from dimers to higher order oligomers. Potential mechanism(s) for the **Tween** 20 effects were investigated. However, no evidence of thermodynamic stabilization of anti-L-selectin conformation (e.g., by **Tween** 20 binding) could be detected. .COPYRGT. 2001 Wiley-Liss, Inc.

L13 ANSWER 9 OF 29 MEDLINE DUPLICATE 2
ACCESSION NUMBER: 2001609128 IN-PROCESS
DOCUMENT NUMBER: 21539437 PubMed ID: 11683251
TITLE: Effect of moisture on the stability of a **lyophilized** humanized monoclonal **antibody** formulation.
AUTHOR: Breen E D; Curley J G; Overcashier D E; Hsu C C; Shire S J
CORPORATE SOURCE: Pharmaceutical Research and Development, Genentech, Inc., South San Francisco, CA 94080, USA.. breen.deirdre@gene.com
SOURCE: PHARMACEUTICAL RESEARCH, (2001 Sep) 18 (9) 1345-53. Journal code: PHS; 8406521. ISSN: 0724-8741.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: IN-PROCESS; NONINDEXED; Priority Journals
ENTRY DATE: Entered STN: 20011102
Last Updated on STN: 20011102
AB PURPOSE: To determine the effect of moisture and the role of the glass transition temperature (Tg) on the stability of a high concentration, **lyophilized**, monoclonal **antibody**. METHODS: A humanized monoclonal **antibody** was **lyophilized** in a **sucrose**/histidine/ **polysorbate** 20 formulation. Residual moistures were from 1 to 8%. Tg values were measured by modulated DSC. Vials were stored at temperatures from 5 to 50 degrees C for 6 or 12 months. Aggregation was monitored by size exclusion chromatography and Asp isomerization by hydrophobic interaction chromatography. Changes in secondary structure were monitored by Fourier transform infrared (FTIR). RESULTS: T. values varied from 80 degrees C at 1% moisture to 25 degrees C at 8% moisture, there was no cake collapse and were

no differences in the secondary structure by FTIR. All formulations were stable at 5 degrees C. High moisture cakes had higher aggregation rates than drier samples if stored above their Tg values. Intermediate moisture vials were more stable to aggregation than dry vials. High moisture samples had increased rates of Asp isomerization at elevated temperatures both above and below their Tg values. Chemical and physical degradation pathways followed Arrhenius kinetics during storage in the glassy state. Only Asp isomerization followed the Arrhenius model above the Tg value. Both chemical and physical stability at T > or = Tg were fitted to Williams-Landel-Ferry (WLF) kinetics. The WLF constants were dependent on the nature of the degradation system and were not characteristic of the solid system. CONCLUSION: High moisture levels decreased chemical stability of the formulation regardless of whether the protein was in a glassy or rubbery state. In contrast, physical stability was not compromised, and may even be enhanced, by increasing residual moisture if storage is below the Tg value.

L13 ANSWER 10 OF 29 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 2000:366976 BIOSIS
DOCUMENT NUMBER: PREV200000366976
TITLE: **Lyophilized** imaging agent formulation comprising a chemotactic peptide.
AUTHOR(S): Corbo, Diane C.; Link, Mary Jean M. (1); Williams, N. Adeyink; Tomsho, Michelle L.; Bornstein, Michael; Solomon, Howard F.; Larsen, Scott K.; Suddith, Robert L.
CORPORATE SOURCE: (1) Princeton, NJ USA
ASSIGNEE: Ortho Pharmaceutical Corporation, Raritan, NJ, USA; Johnson-Matthey Inc., West Chester, PA, USA
PATENT INFORMATION: US 6024938 February 15, 2000
SOURCE: Official Gazette of the United States Patent and Trademark Office Patents, (Feb. 15, 2000) Vol. 1231, No. 3, pp. No pagination. e-file.
ISSN: 0098-1133.
DOCUMENT TYPE: Patent
LANGUAGE: English
AB A **lyophilized** imaging agent formulation and methods for making same are disclosed, such formulations comprise a targeting molecule such as **antibody** or chemotactic peptide, a linker such as diethylenetriaminepentaacetic acid (DTPA) or succinimidyl 6-hydrazinium nicotinate hydrochloride (SHNH), drying protectant such as mannitol, **maltose** or tricine, and excipient such as **polysorbate** 80, in citrate buffer. The formulations of the invention are **lyophilized** and may be stored stably for extended periods of time. Following reconstitution with diluent, the formulations are administered to a subject for scintigraphic imaging or therapeutic use. Also contemplated is a kit comprising a two-vial system wherein a first vial comprises a **lyophilized** formulation of imaging agent in the form of a **lyophilized** cake, and a second vial comprises a pharmaceutically acceptable carrier or diluent.

L13 ANSWER 11 OF 29 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
ACCESSION NUMBER: 2000-679727 [66] WPIDS
DOC. NO. CPI: C2000-206815
TITLE: Parenteral medicinal compositions containing humanized monoclonal **antibody** fragments

stabilized by blending with non-ionic **surfactants** and **sugars** at weakly acidic state, free from restrictions in usage e.g. storage.

DERWENT CLASS: B04 D16
INVENTOR(S): KOBAYASHI, M; MORI, A; OKADA, A
PATENT ASSIGNEE(S): (YAMA) YAMANOUCHI PHARM CO LTD
COUNTRY COUNT: 92
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2000066160	A1	20001109	(200066)*	JA	20

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW

AU 2000043149 A 20001117 (200111)

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2000066160	A1	WO 2000-JP2784	20000427
AU 2000043149	A	AU 2000-43149	20000427

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 2000043149	A	Based on	WO 200066160

PRIORITY APPLN. INFO: JP 1999-121424 19990428
AN 2000-679727 [66] WPIDS
AB WO 200066160 A UPAB: 20001219

NOVELTY - A parenteral medicinal composition containing humanized monoclonal **antibody** fragments, non-ionic **surfactant** and **sugars** with the pH adjusted to weakly acidic, is new.

DETAILED DESCRIPTION - A parenteral medicinal composition containing humanized monoclonal **antibody** fragments, non-ionic **surfactants** and **sugars** with pH adjusted to weakly acidic.

INDEPENDENT CLAIMS are also included for the following:

(i) a drug preparation for parenteral application which is the **freeze-dried** material of the composition; and

(ii) a stabilization method for humanized monoclonal **antibody** fragments, comprising blending them with non-ionic **surfactants** and **sugars** at weakly acidic pH.

ACTIVITY - Anticoagulant.

MECHANISM OF ACTION - **Antibody** inhibition of platelet aggregation.

USE - The composition is used to inhibit blood platelet aggregation.

ADVANTAGE - The composition is stable and free from

restrictions in usage e.g. storage, transportation and handling.

DESCRIPTION OF DRAWING(S) - A simplified production process of a humanized monoclonal **antibody** fragment.

Dwg.1/2

L13 ANSWER 12 OF 29 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
ACCESSION NUMBER: 2001-033775 [05] WPIDS
DOC. NO. CPI: C2001-010403
TITLE: New antisense oligonucleotide against dystrophin pre-mRNA exon 19, useful for treating human Duchenne muscular dystrophy patients with loss of exon 20 in dystrophin mature mRNA.
DERWENT CLASS: A96 B04 D16
INVENTOR(S): MATSUO, M
PATENT ASSIGNEE(S): (JCRP-N) JCR PHARM CO LTD; (MATS-I) MATSUO M; (NICH-N) JAPAN CHEM RES CO LTD
COUNTRY COUNT: 26
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
EP 1054058	A1	20001122	(200105)*	EN	16
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI					
JP 2000325085 A		20001128	(200110)		11

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
EP 1054058	A1	EP 2000-110231	20000518
JP 2000325085 A		JP 1999-140930	19990521

PRIORITY APPLN. INFO: JP 1999-140930 19990521
AN 2001-033775 [05] WPIDS
AB EP 1054058 A UPAB: 20010124

NOVELTY - Use of an antisense oligonucleotide (I) in the manufacture of a therapeutic pharmaceutical composition (II) or medicament for Duchenne muscular dystrophy (DMD) in a human patient with entire loss of exon 20 in the dystrophin mature mRNA, is new. (I) consists of a 20-50 nucleotide sequence against exon 19 of the dystrophin pre-mRNA.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for (II) for DMD in patients with entire loss of exon 20 in the production dystrophin mature mRNA.

ACTIVITY - Relaxant.

MECHANISM OF ACTION - Antisense therapy.

Restores reading frame of dystrophin mature mRNA. A specimen of muscular tissue was taken from a patient who lacked exon 20 in dystrophin gene, minced and trypsinized to give isolated cells. The cells were washed and then cultured in a growth medium and then subcultivated. When the proportion of myoblasts reached about 80%, the medium was replaced with Fusion medium to induce differentiation into muscular cells. On the fourth day of induction of differentiation, antisense oligoDNA (200 pmol) was introduced into the cells using LipofectAMINE and further cultured for 3.7 and 10 days. After respective incubations, the cells were subjected to

immunohistochemical staining using an **antibody** against the C-terminus of dystrophin. It was found that dystrophin staining turned positive in the cells in which no dystrophin staining had initially been detected. In addition, staining with an **antibody** against the N-terminal region of dystrophin also gave a similar result to that obtained with the C-terminal staining, thus confirming that the produced dystrophin extended from the N-terminus to the C-terminus. RNA was extracted from which cDNA was synthesized and amplification comprising a region covering dystrophin exons 18-21 was carried out. The amplification product was sequenced. Results showed that the product had an amino acid reading frame which had been turned in-frame by a direct connection of the exon 18 sequence to that of exon 21 since the fourth day of culture.

USE - In the preparation of medicament and therapeutic composition for DMD in human patients with loss of exon 20 in mature mRNA (claimed). (I) is also useful for treating a human patient with DMD.

ADVANTAGE - (I) shifts the amino acids reading frame in DMD mRNA having an entire loss of exon 20, from an abnormal out-of-frame position, to an in-frame position which converts the disease to the less severe Becker muscular dystrophy.

Dwg.0/0

L13 ANSWER 13 OF 29 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.

ACCESSION NUMBER: 2000084305 EMBASE

TITLE: Development of a **lyophilization** formulation that preserves the biological activity of the platelet-inducing cytokine interleukin-11 at low concentrations.

AUTHOR: Page C.; Dawson P.; Woollacott D.; Thorpe R.; Mire-Sluis A.

CORPORATE SOURCE: C. Page, Division of Immunobiology, NIBSC, Blanche Lane, South Mimms, Potters Bar, Hertfordshire, United Kingdom

SOURCE: Journal of Pharmacy and Pharmacology, (2000) 52/1 (19-26).
Refs: 20
ISSN: 0022-3573 CODEN: JPPMAB

COUNTRY: United Kingdom

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 039 Pharmacy
037 Drug Literature Index

LANGUAGE: English

SUMMARY LANGUAGE: English

AB Recombinant human interleukin-11 (rhIL-11) is a licensed biological therapeutic product in at least one country and is used to combat thrombocytopenia during chemotherapeutic regimens, as well as undergoing clinical trials for a range of other disorders. Following attempts to **lyophilize** IL-11 at low concentrations, it was clear that a significant loss of recoverable biological activity occurred. Investigation of a variety of factors, including the type of container in which the rhIL-11 was **lyophilized**, revealed that surface adsorption to glass was a major factor resulting in loss of activity of rhIL-11 in solution (> 40% reduction after 3 h at room temperature), in addition to losses of activity post-**lyophilization**. To overcome this problem, different formulations containing combinations of human serum

albumin (HSA), **trehalose** and **Tween**-20 have been investigated. Two formulations were successful in entirely preserving the biological activity of rhIL-11 through **lyophilization** and subsequent reconstitution (potency estimates of formulated relative to original material being .gtoreq.0.97). Accelerated degradation studies, performed at intervals over a six-month period, demonstrated the stability of **freeze-dried** rhIL-11 using these formulations (predicted annual reduction in potency after storage at -20.degree.C .ltoreq.1.4%). In conclusion, we have developed a working combination of excipients (0.5% HSA, 0.1% **trehalose** and 0.02% **Tween**-20 in potassium phosphate buffer (pH 7.4)) to formulate a stable rhIL-11 **freeze-dried** product in glass containers, with no loss in potency. These findings should facilitate development of low dose rhIL-11 products and be an indicator of caution to those using this and other material with similar physical properties, without taking appropriate precautions to avoid losses through adsorption.

L13 ANSWER 14 OF 29 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
ACCESSION NUMBER: 1999-302473 [25] WPIDS
DOC. NO. CPI: C1999-088642
TITLE: Preparation of micro- and nano- particle delivery system.
DERWENT CLASS: A96 B04 B07
INVENTOR(S): PROKOP, A
PATENT ASSIGNEE(S): (UYVA-N) UNIV VANDERBILT
COUNTRY COUNT: 22
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9918934	A1	19990422	(199925)*	EN	52
RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE					
W: AU CA JP					
AU 9897991	A	19990503	(199937)		
EP 1021168	A1	20000726	(200037)	EN	
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE					

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 9918934	A1	WO 1998-US21455	19981009
AU 9897991	A	AU 1998-97991	19981009
EP 1021168	A1	EP 1998-952243	19981009
		WO 1998-US21455	19981009

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 9897991	A	Based on	WO 9918934
EP 1021168	A1	Based on	WO 9918934

PRIORITY APPLN. INFO: US 1997-62943P 19971009
AN 1999-302473 [25] WPIDS
AB WO 9918934 A UPAB: 20011203

NOVELTY - A method of making particles useful in drug delivery comprises contacting polyanionic polymers with cations in a stirred reactor so that the polyanions and the cations react to form particles, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) a multicomponent system to generate microparticles, composed of a structural (gelling) polymer and a polymer providing mechanical strength and permeability control;

(2) a particle made by the above method comprising of multicomponent core anionic polymers and anionic antigen, where all components of the core are incorporated as an integral part of the complex formed with the receiving bath polycations;

(3) a composition of matter comprising multicomponent core polymers, where corona polymers also include a charged surface modifier (electrostatic stabilizer) of the same charge as the corona polymers, and in which all corona components are incorporated in one step as an integral part of the complex;

(4) a nonionic polymeric surface modifier (steric stabilizer) as part of the corona multipolymeric system, where all corona components are integrated into the outer polymer structure (shell);

(5) a vaccine comprising the particles of (2);

(6) a composition of matter comprising core anionic polymers and anionic antigens (or plasmid DNA or antisense RNA oligonucleotide), all components being incorporated into the ionically formed complex;

(7) a method of processing reactor content to remove unwanted residual reactants comprises sedimenting or centrifuging the reactor contents, collecting microparticles or nanoparticles generated, rinsing the particles in excess water, buffer or cryopreservation solution, separating suspension by sedimentation or centrifugation, repeating rinsing and separation steps and reducing volume of the suspension to about 1/100th of the initial volume;

(8) a method of chemical stabilization of the washed and isolated particles, by reacting particles with a crosslinking agent, rinsing in excess of water, buffer, or cryopreservation solution, separating the particles by sedimentation or centrifugation, repeating the rinsing and separation as needed, and reducing the volume of the suspension;

(9) a method of cryoprotecting the washed particles, by suspending the particles in a cryoprotective solution, and **lyophilising**;

(10) a method of immunization of animals comprising the step of orally delivering an encapsulated antigen in the particles, where the particles are taken up by M-cells in Peyer's patches of the epithelial lining of the upper intestinal tract resulting in an increase in secretory and systemic **antibodies** in blood;

(11) a method of adjusting the biodegradability of polymeric mixtures, by contacting an enzyme with a polysaccharide, and degrading the substrate at physiological conditions in vivo; and

(12) a method of introducing an adjuvant to potentiate an immunogenic effect, by administration of the adjuvant as part of a droplet forming polymeric mixture.

USE - Possible uses of the micro- or nano- particulate product range over the fields of pharmaceuticals, proteins, polymers, and colloids, immunology, and biomedical engineering. They include delivery of drugs generally, antigens and vaccines for immunization of humans and other animals, genes (plasmid DNA), and antisense RNA

and DNA oligonucleotides. Some targeting is possible, e.g., by adding mocoadhesive polymers to provide sticking to certain mucosal areas; this applies particularly to the M-cells in Peyer's patches in the epithelial lining of the small intestine, to increase delivery of large molecules, e.g., **antibodies**. It is stated that the particle production operation can be carried out as a continuous, in addition to a batch process.

L13 ANSWER 15 OF 29 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
ACCESSION NUMBER: 1999-290190 [25] WPIDS
DOC. NO. CPI: C1999-085883
TITLE: Inhibiting aggregate formation in reconstituted protein **lyophilizates** using potassium phosphate buffer.
DERWENT CLASS: B04 D16
INVENTOR(S): HELLERBRAND, K; PAPADIMITRIOU, A; WINTER, G
PATENT ASSIGNEE(S): (BOEF) BOEHRINGER MANNHEIM GMBH; (HOFF) ROCHE DIAGNOSTICS GMBH
COUNTRY COUNT: 34
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
EP 917879	A2	19990526	(199925)*	GE	11
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI					
AU 9894060	A	19990610	(199934)		
ZA 9810650	A	19990728	(199935)		21
CN 1220270	A	19990623	(199943)		
CA 2254145	A1	19990522	(199945)	EN	
JP 11240895	A	19990907	(199947)		11
AU 714264	B	19991223	(200011)		
BR 9805021	A	20000321	(200028)		
KR 99045460	A	19990625	(200036)		
JP 3105494	B2	20001030	(200057)		10
US 6238664	B1	20010529	(200132)		
MX 9809774	A1	20000801	(200137)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
EP 917879	A2	EP 1998-121684	19981113
AU 9894060	A	AU 1998-94060	19981120
ZA 9810650	A	ZA 1998-10650	19981120
CN 1220270	A	CN 1998-122531	19981120
CA 2254145	A1	CA 1998-2254145	19981120
JP 11240895	A	JP 1998-332681	19981124
AU 714264	B	AU 1998-94060	19981120
BR 9805021	A	BR 1998-5021	19981123
KR 99045460	A	KR 1998-49921	19981120
JP 3105494	B2	JP 1998-332681	19981124
US 6238664	B1	US 1998-196090	19981119
MX 9809774	A1	MX 1998-9774	19981123

FILING DETAILS:

PATENT NO	KIND	PATENT NO

AU 714264 B Previous Publ. AU 9894060
JP 3105494 B2 Previous Publ. JP 11240895

PRIORITY APPLN. INFO: EP 1998-102846 19980219; EP 1997-120528 19971122
AN 1999-290190 [25] WPIDS
AB EP 917879 A UPAB: 20011203
NOVELTY - Improved method for inhibiting formation of protein aggregates in a reconstituted **lyophilizate** of a pharmaceutical protein-containing composition comprises dissolving the protein in an aqueous solution that contains potassium phosphate (I) as buffering agent and has potassium to sodium ion ratio 10:1 or greater.

DETAILED DESCRIPTION - The solution is frozen, thawed, divided into containers, each containing a dose for injection, then **lyophilized**.

INDEPENDENT CLAIMS are also included for the following:

(1) thawable, solid storage form of a protein, with low content of aggregates, that is essentially amorphous, contains a frozen solution of protein in (I) buffer and has K:Na ion ratio at least 10:1; and

(2) a pharmaceutical composition comprising a protein in aqueous buffer of pH 6-8 that contains (I) as buffering agent, has K:Na ion ratio at least 10:1 and has buffer concentration 10-300 mM.

ACTIVITY - None given.

MECHANISM OF ACTION - None given.

USE - The method is preferably used with **antibodies**, particularly those produced by in vitro cell cultures, but may also be applied to immunotoxins, enzymes, protein hormones etc.

ADVANTAGE - The specified buffer stabilizes proteins during freezing, **lyophilization**, and low temperature storage, so that when reconstitutued the solution formed is practically free from aggregates and particles. It allows proteins that tend to dimerize or multimerize at neutral pH to be formulated as stable frozen compositions.

L13 ANSWER 16 OF 29 MEDLINE DUPLICATE 3
ACCESSION NUMBER: 1999417802 MEDLINE
DOCUMENT NUMBER: 99417802 PubMed ID: 10486434
TITLE: Niosomes as a novel peroral vaccine delivery system.
AUTHOR: Rentel C O; Bouwstra J A; Naisbett B; Junginger H E
CORPORATE SOURCE: Leiden/Amsterdam Center for Drug Research, Division of Pharmaceutical Technology, P.O. Box 9502, NL-2300 RA, Leiden, The Netherlands.
SOURCE: INTERNATIONAL JOURNAL OF PHARMACEUTICS, (1999 Sep 20) 186 (2) 161-7.
Journal code: DA4; 7804127. ISSN: 0378-5173.
PUB. COUNTRY: Netherlands
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199912
ENTRY DATE: Entered STN: 20000113
Last Updated on STN: 20000113
Entered Medline: 19991215
AB The feasibility to develop a peroral vaccine delivery system based on non-ionic **surfactant** vesicles (niosomes) was evaluated

using BALB/c mice. Ovalbumin was encapsulated in various **lyophilized** niosome preparations consisting of **sucrose** esters, cholesterol and dicetyl phosphate. Two different formulations were compared in this study. The specific **antibody** titres within serum, saliva and intestinal washings were monitored by ELISA on days 7, 14, 21 and 28 after intragastric administration. Only encapsulation of ovalbumin into Wasag7 (70% stearate **sucrose** ester, 30% palmitate **sucrose** ester (40% mono-, 60% di/tri-ester)) niosomes resulted in a significant increase in **antibody** titres. Administration of ovalbumin and empty niosomes did not exert a similar effect, neither did administration of any control formulation. In contrast to ovalbumin loaded Wasag7 niosomes, application of the more hydrophilic Wasag15 (30% stearate **sucrose** ester, 70% palmitate **sucrose** ester (70% mono-, 30% di/tri-ester)) niosome preparations did not result in an increase in **antibody** titres.

L13 ANSWER 17 OF 29 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
ACCESSION NUMBER: 1998-387644 [33] WPIDS
DOC. NO. NON-CPI: N1998-302308
DOC. NO. CPI: C1998-117205
TITLE: New water soluble vinyl membrane-polymer protein complexes - useful for producing reagent and diagnosis kits, e.g. for immunoassays.
DERWENT CLASS: A14 A96 B04 D16 J04 S03
INVENTOR(S): AUDEBERT, R; POPOT, J; TRIBET, C
PATENT ASSIGNEE(S): (CNRS) CENT NAT RECH SCI; (CNRS) CNRS CENT NAT RECH SCI
COUNTRY COUNT: 19
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9827434	A1	19980625	(199833)*	FR	22
RW: AT BE CH DE DK ES FI FR GB GR IE IT LU MC NL PT SE					
W: JP US					
EP 946875	A1	19991006	(199946)	FR	
R: DE FR GB IT					

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 9827434	A1	WO 1996-FR2009	19961216
EP 946875	A1	EP 1996-942413	19961216
		WO 1996-FR2009	19961216

FILING DETAILS:

PATENT NO	KIND		PATENT NO
EP 946875	A1	Based on	WO 9827434

PRIORITY APPLN. INFO: WO 1996-FR2009 19961216
AN 1998-387644 [33] WPIDS
AB WO 9827434 A UPAB: 19980826
New water soluble vinyl membrane-polymer protein amphiphilic

complexes (A) are claimed, in which the vinyl polymer is of formula (I). R1 = COOM, COOR7, N-pyrrolidonyl, phenyl sulphonate or CONR8R9; M = alkali cation; R7 = **sugar** residue, polyoxyalkylene (preferably polyoxyethylene) with 4-10 alkylene oxide units or (CH2)t-NR10R11; R8, R9 = H, **sugar** residue, zwitterionic radical or polyoxyalkylene (preferably polyoxyethylene) with 4-10 alkylene oxide units; t = 1-5; R10, R11 = H or 1-4C alkyl; R4-R6 = H or methyl; R2 = COOR12 or CONR13R14; R12 = 6-12C alkyl or alkenyl; R13, R14 = 6-12C alkyl or alkenyl, or one of them may also be H; R3 = COOR15 or CONR16R17; R15 = 1-5C alkyl; R16, R17 = 1-5C alkyl, or one of them may also be H; x,y,z are the percentages of the respective repeating units; x = 20-90%; y = 10-80%; z = 0-60%; the average molecular weight is 500-100,000, preferably 50,000 or less.

USE - Reagent kits and immunological diagnostic kits containing (A) are claimed. (A) can be used: to simplify manipulation of protein solutions; to enable proteins to be studied by methods impossible in the presence of **surfactants** or lipid membranes (e.g. NMR in liquid media, crystallography or electron microscopy of certain types); to obtain concentrated protein solutions (e.g. 10g/l); for storage in **lyophilised** form, followed by resuspension by simple addition of water or buffer; in diagnostic systems utilising the membrane proteins as receptors or antigens, e.g. for research into circulating **antibodies**, both soluble or carried by lymphocytes; and in immunisation and the production of **antibodies**, and to amplify the immune response. The membrane proteins include enzymes, the complexation of which by (I) has potential industrial use. The absence of **surfactant** enables many pharmacological test to be simplified, e.g. measurement of the affinity of cellular receptors for drugs.

ADVANTAGE - (A) can be **lyophilised** or made into concentrated solutions; (A) in **lyophilised** form and aqueous solutions containing (A) at > 5g/l (preferably 10-500 g/l) are claimed. (A) do not contain **surfactants**. They are stable for several weeks in solution, degradation being comparable with that of proteins in conventional micellar media. The native form of proteins is preserved.

Dwg.0/2

L13 ANSWER 18 OF 29 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
ACCESSION NUMBER: 1998-312175 [27] WPIDS
DOC. NO. CPI: C1998-096288
TITLE: Stable **lyophilised** composition of monoclonal or polyclonal **antibodies**, - which also contains **sugar** or amino **sugar**, amino acid and **surfactant**, for use as therapeutic or diagnostic agent.
DERWENT CLASS: A96 B04 D16
INVENTOR(S): KALLMEYER, G; KLESSEN, C; WINTER, G; WOOG, H
PATENT ASSIGNEE(S): (BOEF) BOEHRINGER MANNHEIM GMBH; (HOFF) ROCHE DIAGNOSTICS GMBH
COUNTRY COUNT: 80
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9822136	A2	19980528	(199827)*	GE	39

RW: AT BE CH DE DK EA ES FI FR GB GH GR IE IT KE LS LU MC MW NL

OA PT SD SE SZ UG ZW
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI
GB GE GH HU IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD
MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR
TT UA UG US UZ VN YU ZW

EP 852951	A1	19980715 (199832)	GE	
R: DE				
AU 9854841	A	19980610 (199843)		
ZA 9710409	A	19990728 (199935)		39
EP 941121	A2	19990915 (199942)	GE	
R: AT BE CH DE DK ES FI FR GB GR IE IT LI LU NL PT SE				
CN 1244805	A	20000216 (200027)		
BR 9713521	A	20000321 (200028)		
KR 2000053328	A	20000825 (200121)		
JP 2001503781	W	20010321 (200122)		36
MX 9904565	A1	20000701 (200134)		
AU 735411	B	20010705 (200143)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 9822136	A2	WO 1997-EP6452	19971119
EP 852951	A1	EP 1996-118489	19961119
AU 9854841	A	AU 1998-54841	19971119
ZA 9710409	A	ZA 1997-10409	19971119
EP 941121	A2	EP 1997-951238	19971119
		WO 1997-EP6452	19971119
CN 1244805	A	CN 1997-181416	19971119
BR 9713521	A	BR 1997-13521	19971119
		WO 1997-EP6452	19971119
KR 2000053328	A	WO 1997-EP6452	19971119
		KR 1999-704336	19990515
JP 2001503781	W	WO 1997-EP6452	19971119
		JP 1998-523210	19971119
MX 9904565	A1	MX 1999-4565	19990517
AU 735411	B	AU 1998-54841	19971119

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 9854841	A	Based on	WO 9822136
EP 941121	A2	Based on	WO 9822136
BR 9713521	A	Based on	WO 9822136
KR 2000053328	A	Based on	WO 9822136
JP 2001503781	W	Based on	WO 9822136
AU 735411	B	Previous Publ.	AU 9854841
		Based on	WO 9822136

PRIORITY APPLN. INFO: EP 1996-118489 19961119
AN 1998-312175 [27] WPIDS
AB WO 9822136 A UPAB: 19990424
Stable **lyophilised** pharmaceutical composition of monoclonal or polyclonal **antibodies**, contains a **sugar** or amino **sugar**, an amino acid and a **surfactant**.
USE - The composition is used as a therapeutic or diagnostic

agent (claimed).
Dwg.0/0

L13 ANSWER 19 OF 29 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
ACCESSION NUMBER: 1998-163671 [15] WPIDS
DOC. NO. CPI: C1998-052837
TITLE: Humoral immunity restorer - contains lactic acid bacterium.
DERWENT CLASS: B04 D16
PATENT ASSIGNEE(S): (NICH-N) NICHI NICHI SEIYAKU KK
COUNTRY COUNT: 1
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
JP 10029946	A	19980203	(199815)*		4

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
JP 10029946	A	JP 1996-205213	19960715

PRIORITY APPLN. INFO: JP 1996-205213 19960715
AN 1998-163671 [15] WPIDS
AB JP 10029946 A UPAB: 19980410
Humoral immunity restorer contains lactic acid bacterium or its treated product and has an activity of restoring humoral immunity function reduced by a chemical.

ADVANTAGE - A drug of high side effects can be dosed by using the humoral immunity restorer. In an example, Enterococcus faecalis NF-1011 was cultured in a Rogosa liquid medium containing 10 g trypticase, 5 g yeast extract, 3 g tryptose, 3 g monopotassium phosphate, 3 g dipotassium phosphate, 2 g triammonium citrate, 1 g **Tween** 80, 20 g **glucose**, 0.2 g cysteine hydrochloride and 5 ml salt solution in 1000 ml water at 37 deg. C for 10-16 hours. The culture was centrifuged and the microbe body was washed with distilled water twice and suspended in distilled water and heated at 110 deg. C for 10 minutes to prepare dead microbe suspension and then **freeze-dried** to prepare a dry dead microbe body. An **antibody**-producing cell was prepared. The microbe body was mixed with powder CE-2 to 5 % and the mixture was dosed freely to a female mouse. The **antibody**-producing cell was detected by plaque method.
Dwg.0/1

L13 ANSWER 20 OF 29 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
ACCESSION NUMBER: 1997-145374 [13] WPIDS
CROSS REFERENCE: 1997-145380 [13]; 2001-496010 [51]; 2001-496382 [54]
DOC. NO. CPI: C1997-046386
TITLE: New stable reconstituted protein formulations - prepd. from **lyophilised** mixt. of protein and lyoprotectant to provide high protein concn..
DERWENT CLASS: B04 D16
INVENTOR(S): ANDYA, J; CLELAND, J L; HSU, C C; LAM, X M; OVERCASHIER, D E; SHIRE, S J; WU, S S; YANG, J Y

PATENT ASSIGNEE(S): (GETH) GENENTECH INC
COUNTRY COUNT: 72
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9704801	A1	19970213	(199713)*	EN	48
RW: AT BE CH DE DK EA ES FI FR GB GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG					
W: AL AM AT AU AZ BB BG BR BY CA CH CN CZ DE DK EE ES FI GB GE HU IL IS JP KE KG KP KR KZ LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK TJ TM TR TT UA UG UZ VN					
AU 9665992	A	19970226	(199725)		
ZA 9606075	A	19980325	(199819)#		55
NO 9800335	A	19980326	(199823)		
EP 845997	A1	19980610	(199827)	EN	
R: AL AT BE CH DE DK ES FI FR GB GR IE IT LI LT LU LV MC NL PT SE SI					
BR 9609743	A	19990302	(199915)		
JP 11510170	W	19990907	(199947)		69
MX 9800684	A1	19980401	(200004)		
NZ 313503	A	20000128	(200015)		
AU 716785	B	20000309	(200022)		
AU 2000010063	A	20000309	(200022)#		

APPLICATION DETAILS:

PATENT NO	KIND		APPLICATION	DATE
WO 9704801	A1		WO 1996-US12251	19960723
AU 9665992	A		AU 1996-65992	19960723
ZA 9606075	A		ZA 1996-6075	19960717
NO 9800335	A		WO 1996-US12251	19960723
			NO 1998-335	19980126
EP 845997	A1		EP 1996-925497	19960723
			WO 1996-US12251	19960723
BR 9609743	A		BR 1996-9743	19960723
			WO 1996-US12251	19960723
JP 11510170	W		WO 1996-US12251	19960723
			JP 1997-507749	19960723
MX 9800684	A1		MX 1998-684	19980123
NZ 313503	A		NZ 1996-313503	19960723
			WO 1996-US12251	19960723
AU 716785	B		AU 1996-65992	19960723
AU 2000010063	A	Div ex	AU 1996-65992	19960723
			AU 2000-10063	20000112

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 9665992	A	Based on	WO 9704801
EP 845997	A1	Based on	WO 9704801
BR 9609743	A	Based on	WO 9704801
JP 11510170	W	Based on	WO 9704801
NZ 313503	A	Based on	WO 9704801
AU 716785	B	Previous Publ.	AU 9665992
		Based on	WO 9704801

AU 2000010063 A Div ex AU 716785

PRIORITY APPLN. INFO: US 1996-615369 19960314; US 1995-508014 19950727; ZA 1996-6075 19960717; AU 2000-10063 20000112

AN 1997-145374 [13] WPIDS

CR 1997-145380 [13]; 2001-496010 [51]; 2001-496382 [54]

AB WO 9704801 A UPAB: 20010927

(A) A stable isotonic reconstituted formulation comprises a protein in an amt. of at least 50 mg/ml and a diluent, which reconstituted formulation has been prepd. from a **lyophilised** mixt. of a protein and a lyoprotectant, where the protein concn. in the reconstituted formulation is about 2-40 times greater than the protein concn. in the mixt. before **lyophilisation**. Also claimed are: (B) a stable reconstituted formulation comprising an **antibody** in an amt. of at least 50 mg/ml in a diluent, which reconstituted formulation has been prepd. from a **lyophilised** mixt. of an **antibody** and a lyoprotectant, where the **antibody** concn. in the reconstituted formulation is about 2-40 times greater than the **antibody** concn. in the mixt. before **lyophilisation**; (C) a method for preparing a formulation comprising: (a) **lyophilising** a mixt. of a protein and a lyoprotectant; and (b) reconstituting the **lyophilised** mixt. of step (a) in a diluent such that the reconstituted formulation is isotonic and stable and has a protein concn. of at least about 50 mg/ml; (D) an article of mfr. comprising: (a) a container which holds a **lyophilised** mixt. of a protein and a lyoprotectant; and (b) instructions for reconstituting the **lyophilised** mixt. with a diluent to a protein concn. in the reconstituted formulation of at least about 50 mg/ml; (E) a formulation comprising a **lyophilised** mixt. of a lyoprotectant and an **antibody**, where the molar ratio of lyoprotectant:**antibody** is about 100-1500 mole lyoprotectant:1 mole **antibody**; (F) a formulation comprising anti-HER2 **antibody** (5-40 mg/ml), **sucrose** or **trehalose** (10-100 mM), a buffer and a **surfactant**; and (G) a formulation comprising anti-IgE **antibody** (5-40 mg/ml), **sucrose** or **trehalose** (80-300 mM), a buffer and a **surfactant**.

USE - The anti-HER **antibody** formulations **antibody** can be used to treat or prevent cancers. The anti-IgE formulations can be used for the treatment or prophylaxis of e.g. IgE-mediated allergic diseases, parasitic infections, interstitial cystitis and asthma.

ADVANTAGE - The reconstituted formulations can have high protein concns. and are stable at 2-8 deg. C for at least 30 days (pref. at 30 deg. C for at least 1 year).

Dwg.0/19

L13 ANSWER 21 OF 29 BIOSIS COPYRIGHT 2001 BIOSIS

ACCESSION NUMBER: 1996:253251 BIOSIS

DOCUMENT NUMBER: PREV199698809380

TITLE: Development of stable **lyophilized** monoclonal **antibody** formulations: Effect of excipients on stability.

AUTHOR(S): Bam, Narendra; Dal Monte, Paul R.; Duddu, Sarma P.

CORPORATE SOURCE: Pharm. Dev., SmithKline Beecham Pharm., King of Prussia, PA 19406 USA

SOURCE: Abstracts of Papers American Chemical Society, (1996) Vol. 211, No. 1-2, pp. BIOT 143.
Meeting Info.: 211th American Chemical Society National Meeting New Orleans, Louisiana, USA March 24-28, 1996
ISSN: 0065-7727.
DOCUMENT TYPE: Conference
LANGUAGE: English

L13 ANSWER 22 OF 29 MEDLINE DUPLICATE 4
ACCESSION NUMBER: 94365558 MEDLINE
DOCUMENT NUMBER: 94365558 PubMed ID: 8083647
TITLE: Removal/neutralization of hepatitis A virus during manufacture of high purity, solvent/**detergent** factor VIII concentrate.
AUTHOR: Lemon S M; Murphy P C; Smith A; Zou J; Hammon J; Robinson S; Horowitz B
CORPORATE SOURCE: Department of Medicine, University of North Carolina, Chapel Hill 27599-7030.
SOURCE: JOURNAL OF MEDICAL VIROLOGY, (1994 May) 43 (1) 44-9.
Journal code: I9N; 7705876. ISSN: 0146-6615.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199410
ENTRY DATE: Entered STN: 19941021
Last Updated on STN: 19941021
Entered Medline: 19941013

AB Recent reports have suggested an increased risk of type A viral hepatitis in hemophilic patients treated with high purity factor VIII concentrates prepared using ion exchange chromatography coupled with solvent/**detergent** treatment for inactivation of viruses. To determine the capacity for removal or inactivation of hepatitis A virus during the factor VIII manufacturing process, human plasma and various factor VIII production intermediates were spiked with cell culture-propagated virus and subjected to scaled down conditions mimicking the manufacture of solvent/**detergent** factor VIII. The combination of **antibody**-mediated neutralization, cryoprecipitation, anion exchange chromatography, and **lyophilization** in the absence of **sucrose** resulted in a minimal reduction of 5.5 to 8.55 log10 in the infectivity of hepatitis A virus.

L13 ANSWER 23 OF 29 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
ACCESSION NUMBER: 1990-361472 [48] WPIDS
DOC. NO. NON-CPI: N1990-275796
DOC. NO. CPI: C1990-157107
TITLE: **Lyophilised** immuno assay reagent contg. dextrin or **trehalose** stabiliserell culture medium - to prevent agglomeration, immuno reactive material and liq. organic auxiliary, easily dispersed in aq. medium.
DERWENT CLASS: A89 B04 D16 S03
INVENTOR(S): COLE, F X
PATENT ASSIGNEE(S): (HYGE-N) HYGEIA SCI INC; (HYGE-N) HYGEIA SCIENCES LTD
COUNTRY COUNT: 16

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9013637	A	19901115	(199048)*		31
RW: AT BE CH DE DK ES FR GB IT LU NL SE					
W: CA JP					
EP 470192	A	19920212	(199207)		
R: AT BE CH DE ES FR GB IT LI LU NL SE					
US 5102788	A	19920407	(199217)		7
JP 05500854	W	19930218	(199312)		31
EP 470192	A4	19920311	(199521)		
EP 470192	B1	19971008	(199745)	EN	3
R: AT BE CH DE DK ES FR GB IT LI LU NL SE					
DE 69031561	E	19971113	(199751)		
ES 2110415	T3	19980216	(199813)		
JP 2823353	B2	19981111	(199850)		7

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
EP 470192	A	EP 1990-908003	19900416
US 5102788	A	US 1989-344575	19890428
JP 05500854	W	JP 1990-506814	19900416
		WO 1990-US2064	19900416
EP 470192	A4	EP 1990-908003	
EP 470192	B1	EP 1990-908003	19900416
		WO 1990-US2064	19900416
DE 69031561	E	DE 1990-631561	19900416
		EP 1990-908003	19900416
		WO 1990-US2064	19900416
ES 2110415	T3	EP 1990-908003	19900416
JP 2823353	B2	JP 1990-506814	19900416
		WO 1990-US2064	19900416

FILING DETAILS:

PATENT NO	KIND		PATENT NO
JP 05500854	W	Based on	WO 9013637
EP 470192	B1	Based on	WO 9013637
DE 69031561	E	Based on	EP 470192
		Based on	WO 9013637
ES 2110415	T3	Based on	EP 470192
JP 2823353	B2	Previous Publ.	JP 05500854
		Based on	WO 9013637

PRIORITY APPLN. INFO: US 1989-344575 19890428

AN 1990-361472 [48] WPIDS

AB WO 9013637 A UPAB: 19930928

Lyophilised mmixt. for immunoassay comprises (1) at least one dispersible immunoreactive component (I); (2) at least one normally liq. organic component (II) which enhances the performance of the assay, both of these homogeneously distributed throughout the mixt., and (3) sufficient **sugar**, i.e. dextrin or **trehalose**, to prevent aggregation of (II), thus maintaining homogeneity.

(I) is an **antibody** conjugate (AbC), esp. an Ab-gold sol. particle; Ab-solid carrier (esp. latex) particles or an Ab-enzyme conjugate. (II) is an agent which enhances binding, pref. a nonionic, water-soluble polymer (IIa) and/or a **surfactant** (IIb).

USE/ADVANTAGE - Incorporation of (III) improves shelf life (even when stored under hot, humid conditions) and subsequent dispersion of the mixt. in aq. media for carrying out the immunoassay. The mixt. is easily reconstituted to produce a system contg. all ingredients necessary for an assay. The mixts. are used to assay **antibodies**, antigens, etc. e.g. human chorionic gonadotropin (hCG) or Neisseria gonorrhoea, esp. in sandwich immunoassay for home and clinical diagnostic applications. They allow such tests to be done by unskilled users without special equipment.

0/0

ABEQ US 5102788 A UPAB: 19930928

Lyophilised mixt. of immunoassay reagents comprises a homogeneously-distributed dispersible immunoreactive component(s), a liq. organic component homogeneously distributed in the mixt. to enhance the performance of the immunoassay, and a **sugar**, dextrin or **trehalose**, to prevent agglomeration of the organic components during storage and aid their dispersion in aq. medium during assay.

The immunoreactive component may be an **antibody** conjugate or **antibody**-enzyme conjugate. The organic component which enhances binding may be a nonionic water-soluble polymer e.g. polyethylene glycol, PVA, polyvinyl pyrrolidone or dextran and may include a water-soluble nonionic **surfactant** e.g. a polyethylene glycol, p-isooctyl phenyl ether cpd.

ADVANTAGE - A storage-stable immunoassay system of long shelf life is provided.

ABEQ EP 470192 B UPAB: 19971113

A **lyophilised** mixture for use in an immunoassay procedure comprising: at least one dispersible immunoreactive component distributed homogeneously throughout said mixture; at least one organic component distributed homogeneously throughout said mixture, said organic component normally being a liquid at the conditions under which the mixture is stored or retained prior to use and having a property which enhances the performance of the immunoassay by its presence, and a **sugar** comprising dextrin or **trehalose**, said dextrin or **trehalose** being present in said mixture in sufficient quantity to prevent agglomeration of the organic component and thus maintain the homogeneity of the mixture to thereby facilitate storgage and shelf life of the mixture and the eventual dispersion of the mixture in an aqueous medium for conduct of the immunoassay procedure.

Dwg.0/0

L13 ANSWER 24 OF 29 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
ACCESSION NUMBER: 1990-201016 [26] WPIDS
DOC. NO. NON-CPI: N1990-156415
DOC. NO. CPI: C1990-087053
TITLE: **Lyophilised** mixt. for enzyme immunoassay - contg. **antibody** enzyme conjugate, binding enhancing agent, water-soluble nonionic **surfactant** and **sugar** cpd. to give elevated temp. stability.

DERWENT CLASS: A96 B04 D16 S03
INVENTOR(S): BAHAR, I; BLOCK, E; CICIA, N J; COLE, F; COSEO, M; EATON, C A; JONES, W; SIGILLO, E
PATENT ASSIGNEE(S): (HYGE-N) HYGEIA SCIENCES LTD
COUNTRY COUNT: 1
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
US 4931385	A	19900605	(199026)*		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
US 4931385	A	US 1988-275656	19881121

PRIORITY APPLN. INFO: US 1983-473907 19830310; US 1985-747605 19850624; US 1988-275656 19881121
AN 1990-201016 [26] WPIDS
AB US 4931385 A UPAB: 19930928
In a **lyophilised** mixt. for use in an enzyme immunoassay, the mixt. comprising an **antibody**-enzyme conjugate and buffer salts, the improvement is that the enzyme in the conjugate comprises peroxidase and the mixt. further comprises: (a) a binding enhancing agent from PEG, PVA, polyvinyl pyrrolidone (PVP) and dextran; (b) a water-soluble nonionic **surfactant** in amt. sufficient to provide an appropriate amt. of detergency without having a deleterious effect on the conjugate; and (c) dextrin or trahalose in amt. sufficient to prevent discernible concn. gradients of the components in the mixt.; the **lyophilised** mixt having the property of preserving the **antibody** reactivity and the immunologic binding specificity of the conjugate even if the mixt. is exposed to temps. of 80-120 deg.F prior to its use in the immunoassay. Diagnostic kit for ELISA for detection of an antigen in a sample, suitable for home diagnostic applicn. under ambient temp. conditions, comprises the following separately contained components: (1) a solid support precoated with a first **antibody** and subsequently treated with a blocking soln. comprising a mixt. of a blocking agent and a water-soluble **sugar**, the blocking agent being BSA, gelatin, milk protein or non-specific IgG **antibody**; (2) a vial of the above **lyophilised** mixt.; (3) a measuring dispenser for the sample to be assayed; (4) a container comprising a soln. of a buffer and a peroxide; and (5) a container comprising a soln. of a chromogenic substrate of the peroxidase and a solvent; the components being operable at 15 deg.C to less than 37 deg.C, pref. 15-28 deg.C.

USE/ADVANTAGE - Useful for detection of e.g. human chorionic gonadotropin (LCG) in urinee to detect pregnancy, gonococcal bacteria, luteinising hormone, etc. The assay/kit can be used in the home or physician's office and by unskilled personnel. No specialised appts. is needed. Incubation and washing steps are reduced, thus saving time.
0/0

L13 ANSWER 25 OF 29 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
ACCESSION NUMBER: 1989-339969 [46] WPIDS

DOC. NO. CPI: C1989-150711
TITLE: Homogeneous dimeric macrophage column stimulating factor - and storage stable formulations free of high mol.wt. and stable to prolonged storage.
DERWENT CLASS: A96 B04 D16
INVENTOR(S): AMPHLETT, G; MORIN, S H; MORRIS, J P; SCHRIER, J A; WILLIAMS, D F
PATENT ASSIGNEE(S): (GEMY) GENETICS INST INC
COUNTRY COUNT: 16
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 8910407	A	19891102	(198946)*	EN	
RW: AT BE CH DE FR GB IT LU NL SE					
W: AU JP KR					
AU 8935384	A	19891124	(199016)		
EP 411033	A	19910206	(199106)		
R: AT BE CH DE FR GB IT LI LU NL SE					
JP 03504008	W	19910905	(199142)		
KR 9301303	B1	19930225	(199417)		
EP 411033	B1	19940907	(199434)	EN	6
R: AT BE CH DE FR GB IT LI LU NL SE					
DE 68918091	E	19941013	(199440)		
JP 07076178	B2	19950816	(199537)		5
CA 1340269	C	19981215	(199909)#		
US 5888495	A	19990330	(199920)		

APPLICATION DETAILS:

PATENT NO	KIND		APPLICATION	DATE
EP 411033	A		EP 1989-905303	19890427
JP 03504008	W		JP 1989-505062	19890427
KR 9301303	B1		WO 1989-US1694	19890427
			KR 1989-702462	19891227
EP 411033	B1		EP 1989-905303	19890427
			WO 1989-US1694	19890427
DE 68918091	E		DE 1989-618091	19890427
			EP 1989-905303	19890427
			WO 1989-US1694	19890427
JP 07076178	B2		JP 1989-505062	19890427
			WO 1989-US1694	19890427
CA 1340269	C		CA 1989-601348	19890531
US 5888495	A	Cont of	US 1988-197499	19880523
			US 1992-931551	19920818

FILING DETAILS:

PATENT NO	KIND		PATENT NO
EP 411033	B1	Based on	WO 8910407
DE 68918091	E	Based on	EP 411033
		Based on	WO 8910407
JP 07076178	B2	Based on	JP 03504008
		Based on	WO 8910407

PRIORITY APPLN. INFO: US 1988-197499 19880523; US 1988-187802

Searcher : Shears 308-4994

19880429; CA 1989-601348 19890531; US
1992-931551 19920818

AN 1989-339969 [46] WPIDS

AB WO 8910407 A UPAB: 19930923
Homogeneous dimeric M-CSF, characterised by a single peak when assayed by gel filtration chromatography using a gel filtration matrix having a fractionation range of 10-1500 KD, is new. Also claimed is a storage stable **lyophilised** m-CSF formulation comprising 0.1-2.0% of m-CSF, 0.1-9% of a polyoxyethylenic non-ionic **surfactant**, 65-75% glycine, 17-21% **sucrose**, and 4-7% of a buffering agent, having a pH of 6 upon reconstitution.
USE - m-CSF is a regulatory glycoprotein that stimulates hematoporetic cell proliferation and differentiation. When m-CSF is applied to an in vitro colony stimulating assay it results in the formation of predominantly nonocytic lineage type colonies. m-CSF may be used in activating nature white cells in cases of serious infection or as a therapeutic leukopenia. It may also be used for killing tumour cells either alone or by coadministering it with certain **antibodies** directed to tumour-associated antigens.
0/0

ABEQ EP 411033 B UPAB: 19941013
A storage stable **lyophilised** M-CSF formulation of a homogeneous dimeric M-CSF, which is characterised by a single peak when assayed by gel filtration chromatography using a gel filtration matrix having a fractionation range of about 10-1500 kD, comprising about 0.1-10% by weight of M-CSF, about 0.5-20% by weight of a pharmaceutically acceptable polyoxyethylenic non-ionic **surfactant**, about 40-75% by weight glycine, about 15-40% by weight **sucrose** and to about 25% by weight of a pharmaceutically acceptable buffering agent, having a pH of about 6 upon reconstitution.
Dwg.0/0

L13 ANSWER 26 OF 29 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 1989:160335 BIOSIS
DOCUMENT NUMBER: BA87:82436
TITLE: DETECTION OF CMV **ANTIBODY** USING **FREEZE-DRIED** ERYTHROCYTES BY AN INDIRECT HEMAGGLUTINATION TEST.
AUTHOR(S): WANG M; ZHANG Y; GONG Y
CORPORATE SOURCE: DEP. MICROBIOL., ANHUI MED. UNIV., HEFEI.
SOURCE: CHIN J VIROL, (1988) 4 (3), 239-243.
CODEN: BIXUEA.
FILE SEGMENT: BA; OLD
LANGUAGE: Chinese

AB This paper reported a study on the methodology for the detection of cytomegalovirus **antibody** using **freeze-dried** CMV antigen-sensitized sheep RBC (SRBC) by an indirect hemagglutination test. **Freeze-drying** of CMV antigen-sensitized SRBC was carried out in PBS (pH 7.0) containing 5% heat-inactivated normal rabbit serum and 10% **sucrose**. The main obstacle to the use of such SRBC was a nonspecific agglutination occurring after **lyophilization** of CMV-sensitized SRBC. This obstacle can be overcome by adding **Tween** 20 (1/1,000,000) to the phosphate-buffered saline in which the CMV-sensitized SRBC were resuspended for use. The method we established has fairly good reproducibility. The specificity of the method was the same as ELISA and the sensitivity was higher than

the CF.

L13 ANSWER 27 OF 29 JAPIO COPYRIGHT 2001 JPO
ACCESSION NUMBER: 1987-000417 JAPIO
TITLE: COMPOSITION FOR ORAL CAVITY APPLICATION
INVENTOR: ICHIKAWA HIROMICHI; KIYOSHIGE TATSUO; KIKUCHI YASUO
PATENT ASSIGNEE(S): LION CORP, JP (CO 000676)
PATENT INFORMATION:

PATENT NO	KIND	DATE	ERA	MAIN IPC
JP 62000417	A	19870106	Showa	(4) A61K007-16

JP
APPLICATION INFORMATION
ST19N FORMAT: JP1985-138111 19850625
ORIGINAL: JP60138111 Showa
SOURCE: PATENT ABSTRACTS OF JAPAN, Unexamined Applications, Section: C, Sect. No. 425, Vol. 11, No. 167, P. 128 (19870528)
AN 1987-000417 JAPIO
AB PURPOSE: To provide the titled composition effective to suppress the fixation of pathogenic bacteria of periodontosis in oral cavity and prevent the periodontosis, by using the whole cell, pilus or capsule of the pathogenic bacteria of periodontosis as an antigen, immunizing a mammal with the antigen and using the obtained **antibody** in combination with a nonionic **surfactant** as **active** components.
CONSTITUTION: The objective composition contains (A) an **antibody** produced by immunizing a mammal with an antigen comprising the whole cell, pilus or capsule of the pathogenic bacteria of periodontosis (e.g. Bacterroides gingivalis) (preferably compounded with an antiserum or mild containing said **antibody**) and (B) preferably 0.1-5wt% nonionic **surfactant** (preferably fatty acid alkanolamide, **sucrose** fatty acid ester, polyoxyethylene sorbitan fatty acid ester, etc.).

L13 ANSWER 28 OF 29 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
ACCESSION NUMBER: 1985-297784 [48] WPIDS
DOC. NO. CPI: C1985-128762
TITLE: Stabilised compsn. contg. basic protein or poly peptide - with a modified gelatin as stabiliser, esp. for an interferon obtd. by recombinant DNA technology.
DERWENT CLASS: B04 D16
INVENTOR(S): TERANO, Y
PATENT ASSIGNEE(S): (SUNR) SUNTORY LTD
COUNTRY COUNT: 13
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
EP 162332	A	19851127	(198548)*	EN	21
R: AT BE CH DE FR GB IT LI LU NL SE					
JP 60228422	A	19851113	(198601)		
US 4659570	A	19870421	(198718)		

EP 162332 B 19890719 (198929) EN
R: AT BE CH DE FR GB IT LI LU NL SE
DE 3571552 G 19890824 (198935)
JP 04081573 B 19921224 (199304) 9

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
EP 162332	A	EP 1985-105092	19850426
JP 60228422	A	JP 1984-84990	19840426
US 4659570	A	US 1985-727261	19850425
JP 04081573	B	JP 1984-84990	19840426

FILING DETAILS:

PATENT NO	KIND		PATENT NO
JP 04081573	B	Based on	JP 60228422

PRIORITY APPLN. INFO: JP 1984-84990 19840426

AN 1985-297784 [48] WPIDS

AB EP 162332 A UPAB: 19930925
Stabilised compsn. contains a physiologically active basic protein (I) or polypeptide (II) together with a modified gelatin (III).
Pref. the compsn. esp. contains an interferon which is a polypeptide consisting of 146 amino acid residues arranged in the same sequence as in human gamma-interferon or a polypeptide partly deficient of its C terminal and having the activity of human gamma-interferon (IFN-gamma).
(III) is obtd. by (a) decomposing a physically modified gelatin and forming urea bridges by treatment with a diisocyanate; or (b) decomposing the physically modified gelatin and succinylating the prod. with succinic anhydride; or (c) condensing the physically modified gelatin with glyoxal, then oxidising the prod. with H2O2. The physically modified gelatin is easily water soluble and is obtd. by spray-drying or **freeze-drying** a gelatin or drying by radiofrequency induction heating. The compsn. may also contain an antiviral non-ionic **surfactant**, anionic **surfactant**, a human serum albumin, a **sugar**, etc.
An isotonic agent such as an inorganic salt may also be included.
USE/ADVANTAGE - (I) and (II) are esp.obtd. by cultivation of a micro-organism transformed by a recombinant DNA, and they include interferons, interleukin 2, lysozyme and **antibody** complement. (III) is more effective as a stabiliser than prior materials such as human serum albumin.
0/0

ABEQ EP 162332 B UPAB: 19930925
A prepn of stabilised polypeptide having gamma-interferon activity which comprises a polypeptide having gamma-interferon activity and a modified gelatin obtd by (1) hydrolsying a physically modified gelatin and forming urea bridges by treatment with a diisocyanate, or (2) hydrolysing said physically modified gelatin and succinylating the hydrolysis product with succinic anhydride, or (2) condensing said physically modified gelatin with glyoxal and oxidising the condensation product with hydrogen peroxide, said physically modified gelatin being easily water soluble and obtd by spray-drying or **freeze-drying** a telatin, or

drying the same by radiofrequency induction heating.

ABEQ JP 92081573 B UPAB: 19930925

Stabilised prepn. of physiologically active substance comprising a basic protein or a polypeptide and a modified gelatin is claimed. The basic protein or a polypeptide is obtd. from a cultivated prod. of recombined micro-organism made by recombination DNA technology, and the physiologically active substance is an interferon. The interferon is a polypeptide consisting of 146 aminoacid radicals of the same sequence as in human-gamma interferon, or a polypeptide which lacks part or its C terminal and has human gamma-interferon activity.

USE - Method is esp. effective for stabilised prepn. of INF-gamma. (J60228422-A)

ABEQ US 4659570 A UPAB: 19930925

A poplypeptide (PP) having gamma-interferon (GI) activity is stabilised by a gelatin obtd. by (A) decomposing a physically modified gelatin (PMG) and forming urea bridges by treatment with a diisocyanate, (B) decomposing a PMG and succinylating it with succinic anhydride or (C) condensing the PMG with glyoxal and oxidising the condensation product with H2O2. The PMG is readily soluble in water and is obtd. by spray or **freeze drying** a gelatin or drying it by radio-frequency induction heating.

The PP is pref. obtd from a culture of a microorganism transformed by a recombinant DNA, and either has the correct amino acid sequence of human GI or has the activity of human GI. The stabilised PP also contains an antiviral non-ionic **surfactant**, an anionic **surfactant**, a human serum albumin and a **sugar** as well as an isotonic agent, e.g. an inorganid salt.

ADVANTAGE - The PP can be stored for prolonged period at room temp; the stabiliser does not affect the activity of the PP.

L13 ANSWER 29 OF 29 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
ACCESSION NUMBER: 1982-86226E [41] WPIDS
TITLE: Homogeneous bovine, horse and sheep erythrocyte glyco proteins - useful in sensitive diagnostic haemagglutination assays.
DERWENT CLASS: B04 C03 D16 S03
INVENTOR(S): FLETCHER, M A
PATENT ASSIGNEE(S): (UYMI-N) UNIV MIAMI
COUNTRY COUNT: 12
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
EP 61912	A	19821006	(198241)*	EN	39
R: BE CH DE FR GB LI NL SE					
JP 57206694	A	19821218	(198305)		
US 4460694	A	19840717	(198431)		
US 4525459	A	19850625	(198528)		
CA 1198051	A	19851217	(198604)		
EP 61912	B	19870930	(198739)	EN	
R: BE CH DE FR GB LI NL SE					
DE 3277412	G	19871105	(198745)		
JP 05194599	A	19930803	(199335)		16
JP 07035397	B2	19950419	(199520)		15

APPLICATION DETAILS:

PATENT NO	KIND		APPLICATION	DATE
EP 61912	A		EP 1982-301605	19820326
US 4460694	A		US 1982-356348	19820309
US 4525459	A		US 1982-343235	19820127
JP 05194599	A	Div ex	JP 1982-48786	19820326
			JP 1991-216713	19820326
JP 07035397	B2		JP 1982-48786	19820326

FILING DETAILS:

PATENT NO	KIND		PATENT NO
JP 07035397	B2	Based on	JP 57206694

PRIORITY APPLN. INFO: US 1981-247934 19810326; US 1982-343235 19820127; US 1982-356348 19820309; US 1983-343235 19830127

AN 1982-86226E [41] WPIDS

AB EP 61912 A UPAB: 19930915

Homogeneous borine glycoprotein (I) from bovine erythrocytes is new. It has an amino acid compsn., in mole %, of aspartic acid 7.2, threonine 8, serine 7.2, glutamic acid 16.5, proline 12.9, glycine 8.9, alanine 5.6, valine 5.4, methionine 1.2, isoleucine 6.4, leucine 9.2, tyrosine 0.9, phenylalanine 2.8, histidine 1.3, lysine 1.8 and arginine 4.8. The (I) is free from glycolipids and it contains 25% by wt. of carbohydrate comprising hexose, sialic acid, N-acetylgalactosamine and N-acetyl **glucosamine** (molar ratio 1.6:1:0.5:1.1) and 75% protein (I) gives a single band on polyacrylamide gel electrophoresis when stained with Coomassie blue or with HIO4 modified Schiff reagent.

New horse (II) and sheep (III) glycoproteins are also new along with a procedure for diagnosine mononucleosis.

With (I)-(III) in the homogeneous forms, there is at least a 10-fold increase in sensitivity of the diagnostic haemagglutination tests etc. in which they can be used, compared with the use of the prior crude erythrocyte prepns. (II) and (III) interact with peripheral blood lymphocytes to form E rosettes in vitro and so are useful for enumerating rosetting lymphocytes. (I)-(III) are esp. useful in rapid detection and quantification of **antibody** to Epstein-Barr virus.

ABEQ US 4460694 A UPAB: 19930915

Bovine glycoprotein having approx. amino acid compsn. (mol.%): 7.2 threonine, 7.2 serine, 16.5 glutamic acid, 12.9 proline, 8.9 glycine, 5.6 alanine, 5.4 valine, 1.2 methionine, 6.4 isoleucine, 9.2 leucine, 0.9 tyrosine, 2.8 phenylalanine, 1.3 histidine, 1.8 lysine and 4.8 arginine is new.

USE/ADVANTAGE - The bovine glycoprotein can be labelled with a radioisotope, enzyme, chromophore etc. and used in determn. and detection of heterophile antobody of human infectious mononucleosis.

ABEQ US 4525459 A UPAB: 19930915

New horse erythrocyte glycoprotein has amino acid compsn. of 8.1 (mol.)% aspartic acid, 10.6% threonine, 10.8% serine, 9.4% glutamic acid, 12.3% proline, 9.2% glycine, 11.3% alanine, 4.4% valine, 0.8% methionine, 3.5% isoleucine, 8.2% leucine, 1.1% tyrosine, 2.9% phenylalanine, 1.2% histidine, 1.3% lysine and 4.8% arginine.

New sheep erythrocytes glycoprotein has amino acid compsn. of 5.6 (mole.)% aspartic acid, 8.1% threonine, 12.9% serine, 13.0% glutamic acid, 11.6% proline, 7.7% glycine. 9.6% alanine, 6.2% valine, 0.5% methionine, 4.6% isoleucine, 8.3% leucine, 4.6% tyrosine, 1.2% phenylalanine, 1.6% histidine, 3.2% lysine, 4.0% arginine and 0.3% tryptophan.

USE - For detection of infectious mononucleosis heterophile **antibodies** and for prepn. of a stable standardisable reagent for counting rosetting lymphocytes.

ABEQ EP 61912 B UPAB: 19930915

A process for preparing a bovine, horse or sheep erythrocyte glycoprotein, which comprises the steps of: (a) uniformly suspending dried, ground, hemoglobin-free stroma from the appropriate erythrocytes in anhydrous acetone; (b) refluxing for from about 1 to about 6 hours, filtering and drying the residue; (c) suspending said dried residue in 100% anhydrous ethanol; (d) refluxing for from 1 to about 6 hours, filtering and drying the residue; (e) suspending the dried residue from step (d) in aqueous ethanol of from about 50% to about 80% strength and repeating step (b); (f) dissolving the residue from step (e) in water and adding 90% aqueous ethanol, followed by incubating on ice, until crystallisation occurs, centrifuging and dialysing the solid layer against a low pH, low ionic strength buffer; (g) passing the solid from step (f) through a cation exchange resin on a chromatographic column; (h) collecting the sialic acid containing fractions from the column and drying them; (i) treating the collected fractions from step (h) by extraction with a known lipid solvent, centrifuging, collecting the aqueous layer and drying it; (j) repeating step (i) on the product of that step, using a different lipid solvent; and (k) recovering the product of step (j) in **lyophilised** form; characterised in that complex glycolipid is removed from the product of step (k) by: (l) dissolving the product of step (k) in a low ionic strength buffer containing about 1% neutral **detergent**; (m) loading the solution from step (l) on an anion exchange chromatographic column; (n) washing the column thoroughly with low ionic strength buffer; (o) eluting the column with aqueous buffer to high salt concentration; and (p) dialysing the product of step (o) against water and recovering the product in **freeze dried** form.

=> fil hom
FILE 'HOME' ENTERED AT 12:42:29 ON 04 DEC 2001

Nickol
09/308223


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FILE 'REGISTRY' ENTERED AT 12:10:49 ON 04 DEC 2001
                E POLYSORBATE/CN
                E POLYSORBATES/CN
L1              9 S POLYSORBATE ?/CN
                E "POLYOXYETHYLENE-POLYOXYPROPYLENE POLYMER"/CN 5
L2              1 S E3
L3             10 S L1 OR L2

                E TWEEN/CN 5
L5             38 S TWEEN ?/CN

L7             22 S (GLUCOSE OR MANNOSE OR GALACTOSE OR FRUCTOSE OR SORBOSE
                E "N-METHYLGLUCOSAMINE"/CN 5
L8              1 S E3
L9             23 S L7 OR L8

FILE 'CAPLUS' ENTERED AT 12:21:41 ON 04 DEC 2001
L1              9 SEA FILE=REGISTRY ABB=ON  PLU=ON  POLYSORBATE ?/CN
L2              1 SEA FILE=REGISTRY ABB=ON  PLU=ON  "POLYOXYETHYLENE-POLYOX
                  YPROPYLENE POLYMER"/CN
L3             10 SEA FILE=REGISTRY ABB=ON  PLU=ON  L1 OR L2
L4           1260 SEA FILE=CAPLUS ABB=ON  PLU=ON  (LYOPHILIZ? OR LYOPHILIS?
                   OR FREEZ?(W)(DRY? OR DRIED)) AND (MOAB OR MAB OR
                  ANTIBOD?)
L5             38 SEA FILE=REGISTRY ABB=ON  PLU=ON  TWEEN ?/CN
L6             80 SEA FILE=CAPLUS ABB=ON  PLU=ON  L4 AND (L3 OR L5 OR
                  TWEEN OR DETERGENT OR SURFACTANT OR SURFAC?(2A)ACTIVE OR
                  POLYSORBATE OR POLY SORBATE OR (POLYOXYETHYLENE OR
                  POLY(W)(OXYETHYLENE OR OXY ETHYLENE) OR POLYOXY ETHYLENE)
                  (3A)(POLYOXYPROPYLENE OR POLY(W)(OXYPROPYLENE OR OXY
                  PROPYLENE) OR POLYOXY PROPYLENE))
L7             22 SEA FILE=REGISTRY ABB=ON  PLU=ON  (GLUCOSE OR MANNOSE OR
                  GALACTOSE OR FRUCTOSE OR SORBOSE OR SUCROSE OR LACTOSE
                  OR MALTOSE OR CELLOBIOSE OR GENTIOBIOSE OR ISOMALTOSE OR
                  TREHALOSE OR RAFFINOSE OR GLUCOSAMINE OR "N-METHYL-GLUCOS
                  AMINE" OR GALACTOSAMINE OR NEURAMINIC ACID)/CN
L8              1 SEA FILE=REGISTRY ABB=ON  PLU=ON  N-METHYLGLUCOSAMINE/CN

L9             23 SEA FILE=REGISTRY ABB=ON  PLU=ON  L7 OR L8
L10        628644 SEA FILE=CAPLUS ABB=ON  PLU=ON  L9 OR SUGAR OR GLUCOSE
                  OR MANNOSE OR GALACTOSE OR FRUCTOSE OR SORBOSE OR
                  SUCROSE OR LACTOSE OR MALTOSE OR CELLOBIOSE OR GENTIOBIOS
                  E OR ISOMALTOSE OR TREHALOSE OR RAFFINOSE OR GLUCOSAMINE
                  OR METHYLGLUCOSAMINE OR GALACTOSAMINE OR NEURAMINIC
L11            37 SEA FILE=CAPLUS ABB=ON  PLU=ON  L6 AND (L10 OR ?SACCHARID
                  E?)

L11  ANSWER 1 OF 37  CAPLUS  COPYRIGHT 2001 ACS
ACCESSION NUMBER:         2001:800884  CAPLUS
TITLE:                    The effects of Tween 20 and
                          sucrose on the stability of
                          anti-L-selectin during lyophilization
                          and reconstitution
AUTHOR(S):                Jones, Latoya S.; Randolph, Theodore W.;
                          Kohnert, Ulrich; Papadimitriou, Apollon; Winter,
                          G.; Hagmann, Marie-Luise; Manning, Mark C.;
                          Carpenter, John F.
CORPORATE SOURCE:         School of Pharmacy, University of Colorado
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Health Sciences Center, Denver, CO, 80262, USA
SOURCE: J. Pharm. Sci. (2001), 90(10), 1466-1477
CODEN: JPMSAE; ISSN: 0022-3549
PUBLISHER: Wiley-Liss, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB We have chosen an anti-L-selectin **antibody** as a model protein to investigate the effects of **sucrose** and/or **Tween** 20 on protein stability during **lyophilization** and reconstitution. Native anti-L-selectin secondary structure is substantially retained during **lyophilization** in the presence of **sucrose** (1 or 0.125%). However, aggregation of the protein during reconstitution of **lyophilized** protein powders prepd. without **sucrose** is not reduced by the presence of **sucrose** in the reconstitution medium. Aggregate formation upon reconstitution is completely inhibited by **freeze drying** the protein with **sucrose** and reconstituting with a 0.1% **Tween** 20 soln. **Tween** 20 (0.1%) also partially inhibits loss of native anti-L-selectin secondary structure during **lyophilization**. However, upon reconstitution the formulations **lyophilized** with **Tween** 20 contain the highest levels of aggregates. The presence of **Tween** in only the reconstitution soln. appears to inhibit the transition from dimers to higher order oligomers. Potential mechanism(s) for the **Tween** 20 effects were investigated. However, no evidence of thermodn. stabilization of anti-L-selectin conformation (e.g., by **Tween** 20 binding) could be detected.
REFERENCE COUNT: 39
REFERENCE(S): (1) Allison, S; Arch Biochem Biophys 1998, V358, P171 CAPLUS
(2) Allison, S; Arch Biochem Biophys 1999, V365, P289 CAPLUS
(3) Allison, S; Biophys J 1996, V71, P2022 CAPLUS
(5) Arakawa, T; Adv Drug Del Rev 1993, V10, P1 CAPLUS
(7) Bam, N; Biotechnol Prog 1996, V12, P801 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 2 OF 37 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2001:783286 CAPLUS
TITLE: Effect of moisture on the stability of a **lyophilized** humanized monoclonal **antibody** formulation
AUTHOR(S): Breen, E. D.; Curley, J. G.; Overcashier, D. E.; Hsu, C. C.; Shire, S. J.
CORPORATE SOURCE: Pharmaceutical Research and Development, Genentech, Inc., South San Francisco, CA, 94080, USA
SOURCE: Pharm. Res. (2001), 18(9), 1345-1353
CODEN: PHREEB; ISSN: 0724-8741
PUBLISHER: Kluwer Academic/Plenum Publishers
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Purpose. To det. the effect of moisture and the role of the glass transition temp. (Tg) on the stability of a high concn.,

lyophilized, monoclonal **antibody**. Methods. A humanized monoclonal **antibody** was **lyophilized** in a **sucrose**/histidine/**polysorbate** 20 formulation. Residual moistures were from 1 to 8%. Tg values were measured by modulated DSC. Vials were stored at temps. from 5 to 50.degree.C for 6 or 12 mo. Aggregation was monitored by size exclusion chromatog. and Asp isomerization by hydrophobic interaction chromatog. Changes in secondary structure were monitored by Fourier transform IR (FTIR). Results. Tg values varied from 80.degree.C at 1% moisture to 25.degree.C at 8% moisture. There was no cake collapse and were no differences in the secondary structure by FTIR. All formulations were stable at 5.degree.C. High moisture cakes had higher aggregation rates than drier samples if stored above their Tg values. Intermediate moisture vials were more stable to aggregation than dry vials. High moisture samples had increased rates of Asp isomerization at elevated temps. both above and below their Tg values. Chem. and phys. degrdn. pathways followed Arrhenius kinetics during storage in the glassy state. Only Asp isomerization followed the Arrhenius model above the Tg value. Both chem. and phys. stability at T .gtoreq. Tg were fitted to Williams-Landel-Ferry (WLF) kinetics. The WLF consts. were dependent on the nature of the degrdn. system and were not characteristic of the solid system. Conclusion. High moisture levels decreased chem. stability of the formulation regardless of whether the protein was in a glassy or rubbery state. In contrast, phys. stability was not compromised, and may even be enhanced, by increasing residual moisture if storage is below the Tg value.

REFERENCE COUNT: 30

REFERENCE(S):

(2) Bell, L; J Pharm Sci 1995, V84, P707 CAPLUS
(3) Boye, J; J Agricul Food Chem 1997, V45, P1116 CAPLUS
(4) Cacia, J; Biochemistry 1996, V35, P1897 CAPLUS
(5) Carpenter, J; Dev Biol Stand 1992, V74, P225 CAPLUS
(6) Chang, B; Arch Biochem Biophys 1996, V331, P249 CAPLUS

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 3 OF 37 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 2001:780648 CAPLUS
DOCUMENT NUMBER: 135:335147
TITLE: Polymer-based injectable sustained release pharmaceutical compositions for peptide and protein drugs
INVENTOR(S): Lee, Hee-yong; Lee, Hye-suk; Kim, Jung-soo; Kim, Sang-beom; Lee, Ji-suk; Choi, Ho-il; Chang, Seung-gu
PATENT ASSIGNEE(S): Peptron Inc., S. Korea
SOURCE: PCT Int. Appl., 37 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

WO 2001078687 A1 20011025 WO 2001-KR462 20010322

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: KR 2000-20484 A 20000418
KR 2000-49344 A 20000824

AB Controlled and sustained release injectable pharmaceutical compns. for a biopharmaceutical, such as peptides and proteins are described. Processes for prepn. of an injectable sustained release compn. comprises (i) a step of prepg. biodegradable porous microspheres having accessible ionic functional groups, (ii) a step of encapsulating a biopharmaceutical into the microspheres through ionic interaction by suspending or equilibrating the microspheres in a soln. contg. the biopharmaceutical, and (iii) a step of recovering and **freeze-drying** the biopharmaceutical-incorporated microspheres. For example, microspheres were prepd. by water/oil/water double emulsion solvent evapn. method using a hydrophilic 50:50 PLGA polymer (RG 502H), which contains free carboxy end groups. Deionized water (800 mL) was added to 1 g of PLGA polymer dissolved in 2 mL of methylene chloride and emulsified by sonication for 30 s using a probe type ultrasonic generator. This primary emulsion was dispersed into 200 mL of deionized water contg. 0.5% polyvinyl alc. (wt./vol.) in a vessel which connected to a const. temp. controller and mixed well by stirring for 15 min at 2500 rpm, 25.degree. using a mixer. After mixing for another 15 min at 1500 rpm, 25.degree., temp. of continuous phase was increased to 40.degree. to evap. methylene chloride. After 1 h stirring at 40.degree., 1500 rpm, temp. was decreased to 25.degree.. The hardened microspheres were collected by centrifugation and washed twice with 200 mL of deionized water, and then **freeze-dried**. The microspheres obtained were used for incorporation of protein drugs, i.e., ovalbumin, bovine serum albumin, human growth hormone, RNase A, or lysozyme through ionic interaction by simply soaking and equilibrating the microspheres into a buffer soln. having an appropriate concn. of protein.

REFERENCE COUNT: 2

REFERENCE(S): (1) Bodmer; In J Controlled Release 1992, V211-3, P129
(2) Syntex Inc; US 5470582 1995 CAPLUS

L11 ANSWER 4 OF 37 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 2001:50923 CAPLUS

DOCUMENT NUMBER: 134:114834

TITLE: Preparation of **antibody** or antigen spheres for diagnostic tests

INVENTOR(S): Goertz, Susan; Hemmes, Paul

PATENT ASSIGNEE(S): Spectral Diagnostics, Inc., Can.

SOURCE: PCT Int. Appl., 34 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001004633	A2	20010118	WO 2000-IB967	20000714

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 1999-353191 A 19990714
US 2000-616018 A 20000713

AB The invention relates to **surfactant**-free reagent spheres useful for biol. tests particularly those involving antigen/**antibody** reactions. The prepd. **antibody** or antigen spheres are used for detection of microorganism, peptidoglycan, **lipopolysaccharide**, cytokine, interleukin, tumor necrosis factor, drug abuse, or therapeutic agent; and for diagnosis of infection, sepsis, etc. diseases.

IT **50-99-7, Glucose**, biological studies
RL: ANT (Analyte); BSU (Biological study, unclassified); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(prepn. of **antibody** or antigen spheres for diagnostic tests)

IT **99-20-7, Trehalose**
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(prepn. of **antibody** or antigen spheres for diagnostic tests)

L11 ANSWER 5 OF 37 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2001:27412 CAPLUS
DOCUMENT NUMBER: 134:105824
TITLE: CD18- or CD20-binding **antibody** formulation
INVENTOR(S): Lam, Xanthe M.; Oeswein, James Q.; Ongpipattanakul, Boonsri; Shahrokh, Zahra; Wang, Sharon X.; Weissburg, Robert P.; Wong, Rita L.
PATENT ASSIGNEE(S): Genentech, Inc., USA
SOURCE: U.S., 56 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6171586	B1	20010109	US 1998-97171	19980612

PRIORITY APPLN. INFO.: US 1997-53087 P 19970613

AB A stable aq. pharmaceutical formulation comprising a therapeutically effective amt. of an **antibody** not subjected to prior **lyophilization**, a buffer maintaining the pH in the range from about 4.5 to about 6.0, a **surfactant** and a polyol is described, along with uses for such a formulation.

IT **57-50-1, Sucrose**, biological studies
99-20-7, Trehalose
RL: MOA (Modifier or additive use); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(CD18- or CD20-binding **antibody** formulation)

REFERENCE COUNT: 53
REFERENCE(S):
(1) Akers, M; Pharmaceutical Technology 1984, P36 CAPLUS
(2) Albelda; FASEB-J 1990, V4(11), P2868 CAPLUS
(3) Anderson; US 5736137 1998 CAPLUS
(4) Anon; EP 303746 1989 CAPLUS
(6) Anon; WO 8909402 1989 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 6 OF 37 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2000:822526 CAPLUS
DOCUMENT NUMBER: 134:9337
TITLE: Adjuvant optimized for stability and biocompatibility for enhancing humoral and cellular immune responses
INVENTOR(S): Mueller, Rainer Helmut; Grubhofer, Nikolaus; Olbrich, Carsten
PATENT ASSIGNEE(S): Gerbu G.m.b.H., Germany; Pharmasol G.m.b.H.
SOURCE: Ger. Offen., 26 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 10024788	A1	20001123	DE 2000-10024788	20000519
WO 2000071154	A2	20001130	WO 2000-EP4565	20000519
WO 2000071154	A3	20010628		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

WO 2000071077	A2	20001130	WO 2000-EP4644	20000522

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ,

TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

AU 2000058091 A5 20001212 AU 2000-58091 20000522
PRIORITY APPLN. INFO.: DE 1999-19923256 A1 19990520
WO 2000-EP4644 W 20000522

AB A title adjuvant is disclosed for injection in combination with an antigen. The adjuvant consists of solid lipid particles or solid lipid mixts. It can be used for manuf. of efficient and biocompatible vaccines for immunization of human and other animals as well as for the prodn. of **antibodies**. By selection of the particle size, particle charge, and particle surface properties the strength of the immune response can be modulated. The optimized adjuvant can be used in combination with other adjuvants such as mol. adjuvants like GMDP.

IT **9003-11-6, Polyoxyethylene-polyoxypropylene** copolymer **9005-65-6, Tween** 80
RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(adjuvant optimized for stability and biocompatibility for enhancing humoral and cellular immune responses)

L11 ANSWER 7 OF 37 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2000:513486 CAPLUS
DOCUMENT NUMBER: 133:125304
TITLE: Nonaqueous solutions and suspensions of macromolecules for pulmonary delivery
INVENTOR(S): Klibanov, Alexander M.
PATENT ASSIGNEE(S): Massachusetts Institute of Technology, USA
SOURCE: PCT Int. Appl., 12 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000042993	A2	20000727	WO 2000-US957	20000114
WO 2000042993	A3	20001130		

W: CA, JP
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE

PRIORITY APPLN. INFO.: US 1999-116860 P 19990122
US 1999-443716 A 19991119

AB Methods and formulations for delivery of macromols., such as proteins, **polysaccharides**, and nucleic acids, are disclosed, where the macromol. is dissolved or dispersed in a low toxicity org. solvent which can be aerosolized for delivery to a patient's lungs by inhalation. Optionally, appropriate soly. enhancers are also present in the formulations compn.

L11 ANSWER 8 OF 37 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2000:114380 CAPLUS
DOCUMENT NUMBER: 132:171107

TITLE: **Lyophilized** imaging agent formulation comprising a chemotactic peptide

INVENTOR(S): Corbo, Diane C.; Link, Mary Jean M.; Williams, N. Adeyinka; Tomsho, Michelle L.; Bornstein, Michael; Solomon, Howard F.; Larsen, Scott K.; Suddith, Robert L.

PATENT ASSIGNEE(S): Ortho Pharmaceutical Corp., USA; Johnson-Matthey Inc.

SOURCE: U.S., 25 pp., Division of U.S. Ser. No. 271,818, abandoned.
CODEN: USXXAM

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6024938	A	20000215	US 1997-997894	19971224
ZA 9505642	A	19970506	ZA 1995-5642	19950706

PRIORITY APPLN. INFO.: US 1994-271818 B3 19940707

AB A **lyophilized** imaging agent formulation comprises a targeting mol. such as **antibody** or chemotactic peptide, a linker such as diethylenetriaminepentaacetic acid (DTPA) or succinimidyl 6-hydrazinium nicotinate-HCl (SHNH), drying protectant such as mannitol, **maltose** or tricine, and excipient such as **Polysorbate** 80, in citrate buffer. The formulations are **lyophilized** and may be stored for extended periods of time. Following reconstitution with a diluent, the formulations are administered to a subject for scintigraphic imaging or therapeutic use. Also contemplated is a kit comprising a 2-vial system wherein a first vial comprises a **lyophilized** formulation of imaging agent in the form of a **lyophilized** cake, and a second vial comprises a carrier or diluent. The DTPA-IgG imaging agent was **lyophilized** in accordance with the following protocol. One-half (0.5) mL of a 4 mg/mL imaging agent formulation (DTPA-IgG) contg. saline 0.9, **maltose** 5, and **Polysorbate**-80 0.04% and pH 4.5 citrate buffer (80 mM) was **lyophilized**. The formulation was placed in a glass vial and the vial held in the **lyophilizer** at 5.degree. for one-half hour, after which time the temp. was ramped-down over 9 h to -50.degree.. The **lyophilized** vial was reconstituted with 2.0 mL 0.9% saline and the final formulation contained imaging agent 1 mg/mL in 20 mM citrate buffer, 1.25% **maltose**, 0.9% saline and 0.01% **Polysorbate**-80 at pH 4.5.

IT **69-79-4, Maltose 9005-65-6,**
Polysorbate 80
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**lyophilized** imaging agent formulation comprising chemotactic peptide)

REFERENCE COUNT: 45
REFERENCE(S):

(1) Abrams, M; J Nucl Med 1990, V31(12), P2022 CAPLUS
(2) Anon; EP 0314317 A1 1989 CAPLUS
(3) Anon; WO 8911297 1989 CAPLUS
(4) Anon; WO 9104056 1991 CAPLUS
(5) Borrebaeck, C; J Immunol Meth 1989, V123, P157 CAPLUS

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 9 OF 37 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1999:610563 CAPLUS
DOCUMENT NUMBER: 131:241966
TITLE: Stabilization of hepatitis C virus antigen-sensitized latex reagent
INVENTOR(S): Taiheiraku, Yoshihiro; Ifuku, Yasuo; Miyoshi, Kinya; Washisu, Masayoshi
PATENT ASSIGNEE(S): Mitsubishi Chemical Industries Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 5 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 11258241	A2	19990924	JP 1998-56573	19980309

AB Latex particles sensitized with antigen or **antibody** is **freeze-dried** for stable long-term storage. Dispersing agent, stabilizer, carbohydrate, **surfactant** and antioxidant are added for stabilization of the immunoassay reagent. A test kit comprising such latex particles sensitized with hepatitis C virus antigen (esp. C25 antigen) is provided for detecting HCV-specific **antibody** in blood plasma or serum samples.

IT **57-50-1, Sucrose,** analysis
RL: ARU (Analytical role, unclassified); MOA (Modifier or additive use); ANST (Analytical study); USES (Uses)
(stabilization of hepatitis C virus antigen-sensitized latex reagent)

L11 ANSWER 10 OF 37 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1999:581581 CAPLUS
DOCUMENT NUMBER: 132:26728
TITLE: Niosomes as a novel peroral vaccine delivery system
AUTHOR(S): Rentel, C. -O.; Bouwstra, J. A.; Naisbett, B.; Junginger, H. E.
CORPORATE SOURCE: Division of Pharmaceutical Technology, Leiden/Amsterdam Center for Drug Research, Leiden, 2300 RA, Neth.
SOURCE: Int. J. Pharm. (1999), 186(2), 161-167
CODEN: IJPHDE; ISSN: 0378-5173
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The feasibility to develop a peroral vaccine delivery system based on nonionic **surfactant** vesicles (niosomes) was evaluated using BALB/c mice. Ovalbumin was encapsulated in various **lyophilized** niosome prepns. consisting of **sucrose** esters, cholesterol and dicetyl phosphate. Two different formulations were compared in this study. The specific **antibody** titers within serum, saliva and intestinal washings were monitored by ELISA on days 7, 14, 21 and 28 after intragastric administration. Only encapsulation of ovalbumin into Wasag 7 (70% stearate **sucrose** ester, 30% palmitate **sucrose**

ester (40% mono-, 60% di/tri-ester)) niosomes resulted in a significant increase in **antibody** titers. Administration of ovalbumin and empty niosomes did not exert a similar effect, neither did administration of any control formulation. In contrast to ovalbumin loaded Wasag 7 niosomes, application of the more hydrophilic Wasa 15 (30% stearate **sucrose** ester, 70% palmitate **sucrose** ester (70% mono-, 30% di/tri-ester)) niosome prepns. did not result in an increase in **antibody** titers.

IT **57-50-1D**, **Sucrose**, esters
RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(niosomes as peroral vaccine delivery systems)

REFERENCE COUNT: 14
REFERENCE(S):
(1) Alexander, J; WO 93/19781 1993 CAPLUS
(2) Eldridge, J; J Control Release 1990, V11, P205 CAPLUS
(3) Elson, C; J Immunol Methods 1984, V67, P101 CAPLUS
(4) Engvall, E; Methods Enzymol 1980, V70, P419 CAPLUS
(5) Fujii, Y; Immunol Lett 1993, V36, P65 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 11 OF 37 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1999:354978 CAPLUS
DOCUMENT NUMBER: 131:134516
TITLE: **Lyophilization** of Protein Formulations in Vials: Investigation of the Relationship between Resistance to Vapor Flow during Primary Drying and Small-Scale Product Collapse
AUTHOR(S): Overcashier, David E.; Patapoff, Thomas W.; Hsu, Chung C.
CORPORATE SOURCE: Department of Pharmaceutical Research and Development, Genentech Inc., South San Francisco, CA, 94080, USA
SOURCE: J. Pharm. Sci. (1999), 88(7), 688-695
CODEN: JPMSAE; ISSN: 0022-3549
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB During the **lyophilization** process, formulations contg. protein, bulking agent, or lyoprotectant form a dry product layer that can affect the transport of sublimed water vapor. We carried out an investigation of the primary drying segment of **lyophilization** to evaluate the relationship between the resistance to water vapor flow through the dried layer and the microstructure of the dried cake. Recombinant humanized **antibody** HER2 (rhuMAb HER2) formulated in **trehalose** was studied, as were protein-free formulations contg. **trehalose** and **sucrose**. Sublimation rate and product temp. data were used to compute the resistance to mass transfer. Dried cake structure was examd. by SEM and a novel fluorescence microscopy method. Collapse temps. were detd. by **freeze-drying** microscopy. Mass transfer resistance was found to decrease with increases in temp. for each material. Resistance also depended on compn., decreasing in the

formulation series, rhuMAb HER2, **trehalose**, **sucrose**. The **lyophilized** material consisted of porous cakes, with a distinct denser region at the top. Formulation and temp. affected the microstructure of the dried cakes. The formulated **trehalose** and **sucrose** were seen, by both microscopy techniques, to possess small (2-20 .mu.m) holes in their platelike structures after **lyophilization**. The quantity of holes was higher for material dried at higher temp. The collapse temp. (Tc) of a material appeared to play a role in the process, as lower Tc was correlated with lower resistance and a greater extent of holes. Our results are consistent with the theory that lower resistance to water vapor flow in the primary drying stage of **lyophilization** may be due to small-scale product collapse.

IT **57-50-1, Sucrose**, biological studies
99-20-7, Trehalose 9005-64-5,
Polysorbate 20
RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(**lyophilization** of protein formulations in vials)

REFERENCE COUNT: 20
REFERENCE(S):
(1) Carpenter, J; Biochemistry 1989, V28, P3916 CAPLUS
(2) Chang, B; Pharm Res 1995, V12, P831 CAPLUS
(3) Crowe, L; Biophys J 1996, V71, P2087 CAPLUS
(4) Fendly, B; Cancer Res 1990, V50, P1550 CAPLUS
(6) Hsu, C; J Pharm Sci 1996, V85, P70 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 12 OF 37 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1999:344768 CAPLUS
DOCUMENT NUMBER: 130:357132
TITLE: Improved method for stabilizing proteins
INVENTOR(S): Hellerbrand, Klaus; Papadimitriou, Apollon; Winter, Gerhard
PATENT ASSIGNEE(S): Roche Diagnostics G.m.b.H., Germany
SOURCE: Eur. Pat. Appl., 11 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 917879	A2	19990526	EP 1998-121684	19981113
EP 917879	A3	19990609		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
US 6238664	B1	20010529	US 1998-196090	19981119
ZA 9810650	A	19990524	ZA 1998-10650	19981120
AU 9894060	A1	19990610	AU 1998-94060	19981120
AU 714264	B2	19991223		
CN 1220270	A	19990623	CN 1998-122531	19981120
BR 9805021	A	20000321	BR 1998-5021	19981123
JP 11240895	A2	19990907	JP 1998-332681	19981124

JP 3105494 B2 20001030
PRIORITY APPLN. INFO.: EP 1997-120528 A 19971122
EP 1998-102846 A 19980219

AB Formation of protein aggregates in a reconstituted **lyophilizate** of a protein prepn. for pharmaceutical use is prevented by prepg. an aq. soln. of the protein in .gtoreq.10 mM K phosphate buffer (K:Na ratio .gtoreq.10:1), freezing and thawing the soln., dispensing the soln. into injectable doses, and **lyophilizing**. The stabilizing effect of K phosphate buffer is attributed at least in part to their small pH shift during freezing. The protein soln. preferably also contains a nonionic **detergent** (e.g. **polysorbate**) and a cryoprotectant (e.g. a nonreducing **sugar**).

L11 ANSWER 13 OF 37 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1999:7857 CAPLUS
DOCUMENT NUMBER: 130:57165
TITLE: Stabilized **antibody** formulation
INVENTOR(S): Lam, Xanthe M.; Oeswein, James Q.; Ongpipattanakul, Boonsri; Shahrokh, Zahra; Wang, Sharon X.; Weissburg, Robert P.; Wong, Rita L.
PATENT ASSIGNEE(S): Genentech, Inc., USA
SOURCE: PCT Int. Appl., 87 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9856418	A1	19981217	WO 1998-US12209	19980612
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9882559	A1	19981230	AU 1998-82559	19980612
EP 999853	A1	20000517	EP 1998-932747	19980612
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				

PRIORITY APPLN. INFO.: US 1997-874897 19970613
WO 1998-US12209 19980612

AB A stable aq. pharmaceutical formulation comprising a therapeutically effective amt. of an **antibody** not subjected to prior **lyophilization**, a buffer maintaining the pH in the range from about 4.5 to about 6.0, a **surfactant** and a polyol is described, along with uses for such a formulation.

IT **57-50-1, Sucrose**, biological studies
99-20-7, Trehalose
RL: MOA (Modifier or additive use); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(stabilized **antibody** formulation)

REFERENCE COUNT: 6
REFERENCE(S):
(1) Abbott Lab; WO 9641164 A 1996 CAPLUS
(2) Cleland; Critical Reviews in Therapeutic Drug Carrier Systems 1993, V10(4), P307 CAPLUS
(4) Draber, P; Journal of Immunological Methods 1995, V181(1), P37 CAPLUS
(5) Genentech Inc; WO 9704801 A 1997 CAPLUS
(6) Immuno AG; EP 0661060 A 1995 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 14 OF 37 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1998:527193 CAPLUS
DOCUMENT NUMBER: 129:166193
TITLE: Therapeutic treatment and prevention of infections with a bioactive material encapsulated within a biodegradable-biocompatible polymeric matrix
INVENTOR(S): Setterstrom, Jean A.; Van Hamont, John E.; Reid, Robert H.; Jacob, Elliot; Jeyanthi, Ramasubbu; Boedeker, Edgar C.; McQueen, Charles E.; Tice, Thomas R.; Roberts, F. Donald; Friden, Phil
PATENT ASSIGNEE(S): United States Dept. of the Army, USA; Van Hamont, John E.; et al.
SOURCE: PCT Int. Appl., 363 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 10
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9832427	A1	19980730	WO 1998-US1556	19980127
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 6309669	B1	20011030	US 1997-789734	19970127
AU 9863175	A1	19980818	AU 1998-63175	19980127

PRIORITY APPLN. INFO.:

US 1997-789734	A	19970127
US 1984-590308	B1	19840316
US 1992-867301	A2	19920410
US 1995-446148	A2	19950522
US 1995-446149	B2	19950522
US 1996-590973	B2	19960124
WO 1998-US1556	W	19980127

AB Novel burst-free, sustained release biocompatible and biodegradable microcapsules are disclosed which can be programmed to release their active core for variable durations ranging from 1-100 days in an aq. physiol. environment. The microcapsules are comprised of a core of polypeptide or other biol. active agent encapsulated in a matrix of poly(lactide/glycolide) copolymer, which may contain a

pharmaceutically acceptable adjuvant, as a blend of upcapped free carboxyl end group and end-capped forms ranging in ratios from 100/0 to 1/99.

IT **9001-62-1**, Lipase
RL: BPR (Biological process); DEV (Device component use); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(prevention of infections with a bioactive material encapsulated within a biodegradable-biocompatible polymeric matrix)

IT **9005-64-5**, **Tween** 20 **9005-65-6**, **Tween** 80 **9005-67-8**, **Tween** 60
RL: MOA (Modifier or additive use); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(prevention of infections with a bioactive material encapsulated within a biodegradable-biocompatible polymeric matrix)

L11 ANSWER 15 OF 37 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1998:351786 CAPLUS
DOCUMENT NUMBER: 129:32337
TITLE: Stable **lyophilized** pharmaceutical substances from monoclonal or polyclonal **antibodies**
INVENTOR(S): Kallmeyer, Georg; Winter, Gerhard; Klessen, Christian; Woog, Heinrich
PATENT ASSIGNEE(S): Boehringer Mannheim G.m.b.H., Germany; Kallmeyer, Georg; Winter, Gerhard; Klessen, Christian; Woog, Heinrich
SOURCE: PCT Int. Appl., 39 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9822136	A2	19980528	WO 1997-EP6452	19971119
WO 9822136	A3	19980820		
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
EP 852951	A1	19980715	EP 1996-118489	19961119
R: DE				
AU 9854841	A1	19980610	AU 1998-54841	19971119
AU 735411	B2	20010705		
ZA 9710409	A	19990519	ZA 1997-10409	19971119
EP 941121	A2	19990915	EP 1997-951238	19971119
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
CN 1244805	A	20000216	CN 1997-181416	19971119
BR 9713521	A	20000321	BR 1997-13521	19971119

JP 2001503781 T2 20010321 JP 1998-523210 19971119
PRIORITY APPLN. INFO.: EP 1996-118489 A 19961119
WO 1997-EP6452 W 19971119

AB **Lyophilized** therapeutic and diagnostic agents prepd. from monoclonal or polyclonal **antibodies** contain a **sugar** or amino **sugar** as well as an amino acid and a **surfactant** as stabilizers. These **lyophilized** compns. are stable under refrigeration, at room temp., or even at .ltoreq.30.degree. for .ltoreq.2 yr, and are stable after reconstitution with water for injection for .ltoreq.5 days. Thus, a compn. contg. monoclonal **antibody** to hepatitis B virus 8.0, **sucrose** 58.0, arginine 10.0, **Tween** 20 0.1 mg, phosphate buffer 15 mM, NaCl 30 mM, H3PO4 to pH 6.5, and water for injection to 1.0 mL showed satisfactory stability during storage for 4 or 13 wk at 50.degree..

IT **57-50-1, Sucrose,** biological studies
69-79-4, Maltose 99-20-7,
Trehalose 114-04-5, Neuraminic acid
512-69-6, Raffinose 3329-30-4, N-**Methylglucosamine 3416-24-8, Glucosamine**
7535-00-4, Galactosamine 9003-11-6,
Ethylene oxide/propylene oxide copolymer **9005-64-5,**
Tween 20
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(stable **lyophilized** pharmaceutical compns. from monoclonal or polyclonal **antibodies**)

L11 ANSWER 16 OF 37 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1997:394163 CAPLUS
DOCUMENT NUMBER: 127:23753
TITLE: Stabilization of biological materials by drying without freezing
INVENTOR(S): Mattern, Markus; Winter, Gerhard
PATENT ASSIGNEE(S): Boehringer Mannheim Gmbh, Germany
SOURCE: Ger. Offen., 32 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 19539574	A1	19970430	DE 1995-19539574	19951025
WO 9715288	A2	19970501	WO 1996-EP4627	19961024
WO 9715288	A3	19970529		
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM				
CA 2235243	AA	19970501	CA 1996-2235243	19961024
AU 9672984	A1	19970515	AU 1996-72984	19961024
EP 857060	A2	19980812	EP 1996-934811	19961024
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, FI				

CN 1205628	A	19990120	CN 1996-199329	19961024
BR 9611265	A	19990504	BR 1996-11265	19961024
JP 11513700	T2	19991124	JP 1996-516286	19961024
NO 9801868	A	19980625	NO 1998-1868	19980424
PRIORITY APPLN. INFO.:			DE 1995-19539574	19951025
			WO 1996-EP4627	19961024

AB A biol., esp. therapeutic, material is stabilized and preserved by prepg. a soln. of (1) the material, (2) a carbohydrate or a zwitterionic compd. with polar residues, and (3) a zwitterionic compd. with nonpolar residues, and drying the soln. at a temp. above its f.p. The process does not involve use of elevated temps., can be carried out in conventional **lyophilization** app., is energy efficient, and is more rapid than **freeze drying**. Thus, a soln. contg. **maltose** 50, L-phenylalanine 10, L-arginine 10, **polysorbate** 80 0.1, and recombinant human G-CSF 0.35 mg/mL (pH 7.4) was sterilized by filtration and 1-mL portions were dispensed into 2-mL vials fitted with **lyophilization** stoppers and dried isothermally at 20.degree. and reduced pressure for 48 h. The product had a residual water content of 1.16% and a glass transition temp. of 75.degree.. The content of native (monomeric) G-CSF was still 99.83% after 13 wk storage at 50.degree..

IT **57-50-1**, biological studies
RL: MOA (Modifier or additive use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(stabilization of biol. materials by drying without freezing)

L11 ANSWER 17 OF 37 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER:	1997:306965 CAPLUS
DOCUMENT NUMBER:	127:3884
TITLE:	MF59 adjuvant enhances **antibody** responses of infant baboons immunized with Haemophilus influenzae type b and Neisseria meningitidis group C **oligosaccharide** -CRM197 conjugate vaccine
AUTHOR(S):	Granoff, Dan M.; McHugh, Yvonne E.; Raff, Howard V.; Mokatrin, Ahmad S.; Van Nest, Gary A.
CORPORATE SOURCE:	Chiron Vaccines, Emeryville, CA, 94608, USA
SOURCE:	Infect. Immun. (1997), 65(5), 1710-1715 CODEN: INFIBR; ISSN: 0019-9567
PUBLISHER:	American Society for Microbiology
DOCUMENT TYPE:	Journal
LANGUAGE:	English

AB The ability of the adjuvant MF59 to enhance the immunogenicity of **polysaccharide**-protein conjugate vaccines was investigated in infant baboons. MF59 consists of stable droplets (<250 nm) of the metabolizable oil squalene and two **surfactants**, polyoxyethylene sorbitan monooleate and sorbitan trioleate, in an oil-in-water emulsion. In humans, MF59 is well tolerated and enhances the immunogenicity of recombinant protein subunit or particle vaccines. Its effect on the immunogenicity of **polysaccharide**-protein conjugate vaccines is unknown. Baboons 1-4 mo of age were immunized i.m. with N. meningitidis group C and H. influenzae type b (Hib) **oligosaccharide**-CRM197 conjugate vaccines. The **lyophilized** vaccines were reconstituted with phosphate-buffered saline (PBS), Al(OH)3 (alum), or MF59. Groups of 5 animals each were given 3 injections of the resp. formulations, with one injection every 4 wk. Four weeks after

each immunization, the MF59 group had up to 7-fold-higher geometric mean anticapsular-**antibody** titers than the alum group and 5-10-fold higher N. meningitidis group C bactericidal **antibody** titers. Twenty-one weeks after the 3rd immunization, the MF59 group still showed 5-10-fold-higher anticapsular **antibody** titers. The **antibody** responses of the animals given the vaccines reconstituted with PBS were low at all times measured. Both the MF59 and alum groups, but not the PBS group, showed booster **antibody** responses to unconjugated Hib and N. meningitidis group C **polysaccharides** , results consistent with induction of memory B cells. Thus, MF59 may be useful for accelerating and augmenting immunity to **polysaccharide**-protein conjugate vaccines in infants.

L11 ANSWER 18 OF 37 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1997:218669 CAPLUS
DOCUMENT NUMBER: 126:203735
TITLE: Stable isotonic **lyophilized** protein formulation
INVENTOR(S): Andya, James; Cleland, Jeffrey L.; Hsu, Chung C.; Lam, Xanthe M.; Overcashier, David E.; Shire, Steven J.; Yang, Janet Yu-Feng; Wu, Sylvia Sau-Yan
PATENT ASSIGNEE(S): Genentech, Inc., USA
SOURCE: PCT Int. Appl., 48 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9704801	A1	19970213	WO 1996-US12251	19960723
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN				
US 6267958	B1	20010731	US 1996-615369	19960314
CA 2226575	AA	19970213	CA 1996-2226575	19960723
AU 9665992	A1	19970226	AU 1996-65992	19960723
AU 716785	B2	20000309		
EP 845997	A1	19980610	EP 1996-925497	19960723
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI				
CN 1191490	A	19980826	CN 1996-195830	19960723
BR 9609743	A	19990302	BR 1996-9743	19960723
JP 11510170	T2	19990907	JP 1996-507749	19960723
NO 9800335	A	19980326	NO 1998-335	19980126
US 2001014326	A1	20010816	US 2001-809511	20010314

PRIORITY APPLN. INFO.:
US 1995-508014 A 19950727
US 1996-615369 A 19960314
WO 1996-US12251 W 19960723
US 1996-29182 P 19960727

AB A stable **lyophilized** protein formulation is described

which can be reconstituted with a suitable diluent to generate a high protein concn. reconstituted formulation which is suitable for s.c. administration. For example, anti-IgE and anti-HER2 **antibody** formulations have been prepd. by **lyophilizing** these **antibodies** in the presence of a lyoprotectant. The **lyophilized** mixt. thus formed is reconstituted to a high protein concn. without apparent loss of stability of the protein.

IT **57-50-1, Sucrose,** biological studies
99-20-7, Trehalose
RL: MOA (Modifier or additive use); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(stable isotonic **lyophilized** protein formulation)

L11 ANSWER 19 OF 37 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1996:546594 CAPLUS
DOCUMENT NUMBER: 125:242353
TITLE: Preparation of wax beads containing a reagent using liquid nitrogen for cooling and solidifying
INVENTOR(S): Kosak, Kenneth M.; Kosak, Matthew K.
PATENT ASSIGNEE(S): USA
SOURCE: U.S., 14 pp. Cont.-in-part of U.S. 5,413,924.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5550044	A	19960827	US 1994-257567	19940610
US 5413924	A	19950509	US 1992-936357	19920827
US 5968729	A	19991019	US 1998-49707	19980328

PRIORITY APPLN. INFO.:
US 1992-835758 19920213
US 1992-936357 19920827
US 1994-257567 19940610
US 1997-918374 19970826

AB Droplets of molten wax or waxy polymer contg. a reagent are dropped onto the surface of liq. nitrogen, the droplets remain on the surface until solidified, and the droplets are removed from the surface before they sink into the liq. nitrogen to provide beads contg. the reagent. The reagent can be any material that can be entrapped in the beads and does not undergo excessive inactivation when the beads are melted by heating to release the reagent. Examples of reagents are heat-resistant enzymes, enzyme substrates, metal salts, oligonucleotides, inclusion compds., **surfactants,** emulsifiers, antioxidants, stabilizers, drugs, antibiotics, **antibodies** and antigens. An app. for producing the beads contains a plurality of channels through which liq. nitrogen flows from a reservoir. Each channel passes under a dispenser tip from which droplets are formed and released onto the surface of flowing liq. nitrogen. Liq. nitrogen contg. the beads flows from each channel into a pipe and then over a sepn. sieve. The beads can be used in various in vitro chem., biochem. and immunol. reactions including the PCR, where the reagent is released by heating and melting the beads. The beads have all the combined

features for com. use of: (1) spherical shape, (2) uniform, narrow size range (i.e. .ltoreq.5% deviation), (3) free of water contamination, (4) contain an aq. reagent, and (5) can be produced at high speed (i.e. >1000/min).

L11 ANSWER 20 OF 37 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1996:544101 CAPLUS
DOCUMENT NUMBER: 125:177462
TITLE: Surface-modified nanoparticles and method of making and using them
INVENTOR(S): Levy, Robert J.; Labhasetwar, Vinod; Song, Cunxian S.
PATENT ASSIGNEE(S): USA
SOURCE: PCT Int. Appl., 170 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9620698	A2	19960711	WO 1996-US476	19960104
WO 9620698	A3	19980122		
W: AL, AM, AT, AU, CA, CH, CN, CZ, DE, DK, GB, HU, IS, JP, KE, LU, VN, MN, NO, US				
RW: KE, LS, SD, AT, BE, CH, DE, ES, FR, GB, IT, LU, NL, PT, SE, NL, MR, NE, SN				
CA 2207961	AA	19960711	CA 1996-2207961	19960104
AU 9647556	A1	19960724	AU 1996-47556	19960104
EP 805678	A1	19971112	EP 1996-903476	19960104
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE				
JP 10511957	T2	19981117	JP 1996-521279	19960104

PRIORITY APPLN. INFO.: US 1995-369541 19950105
US 1995-389893 19950216
WO 1996-US476 19960104

AB Biodegradable controlled-release nanoparticles as sustained release bioactive agent delivery vehicles include surface modifying agents to target binding of the nanoparticles to tissues or cells of living systems, to enhance nanoparticle sustained release properties, and to protect nanoparticle-incorporated bioactive agents. Unique methods of making small (10 nm to 15 nm, and preferably 20 nm to 35 nm) nanoparticles having a narrow size distribution which can be surface-modified after the nanoparticles are formed is described. Techniques for modifying the surface include a **lyophilization** technique to produce a phys. adsorbed coating and epoxy-derivatization to functionalize the surface of the nanoparticles to covalently bind mols. of interest. The nanoparticles may also comprise hydroxy-terminated or epoxide-terminated and/or activated multiblock copolymers, having hydrophobic segments which may be polycaprolactone and hydrophilic segments. The nanoparticles are useful for local intravascular administration of smooth muscle inhibitors and antithrombogenic agents as part of interventional cardiac or vascular catheterization such as a balloon angioplasty procedure; direct application to tissues and/or cells for gene therapy, such as the delivery of osteotropic genes or gene segments into bone progenitor cells; or

oral administration in an enteric capsule for delivery of protein/peptide based vaccines.

L11 ANSWER 21 OF 37 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1996:516694 CAPLUS
DOCUMENT NUMBER: 125:151116
TITLE: Vaccine adjuvants comprising a sulfolipid **polysaccharides**
INVENTOR(S): Hilgers, Luuk
PATENT ASSIGNEE(S): Solvay et Cie., Belg.
SOURCE: PCT Int. Appl., 29 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9620008	A1	19960704	WO 1995-BE119	19951221
W: AL, AM, AU, BB, BG, BR, BY, CA, CN, CZ, EE, FI, GE, HU, IS, JP, KG, KP, KR, KZ, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TJ, TM, TT, UA, US, UZ, VN				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
BE 1008978	A5	19961001	BE 1994-1174	19941227
CA 2208790	AA	19960704	CA 1995-2208790	19951221
CA 2208849	AA	19960704	CA 1995-2208849	19951221
AU 9643248	A1	19960719	AU 1996-43248	19951221
AU 709104	B2	19990819		
BR 9510223	A	19971230	BR 1995-10223	19951221
EP 814836	A1	19980107	EP 1995-942007	19951221
EP 814836	B1	20010314		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, LT, LV				
CN 1171052	A	19980121	CN 1995-197099	19951221
CN 1175264	A	19980304	CN 1995-197557	19951221
AT 199644	E	20010315	AT 1995-942007	19951221
ES 2155540	T3	20010516	ES 1995-942007	19951221

PRIORITY APPLN. INFO.: BE 1994-1174 A 19941227
WO 1995-BE119 W 19951221

AB Vaccine adjuvants comprising a sulfolipid **polysaccharide** in combination with an interface-forming constituent are claimed. The invention also provides a method for prepg. a vaccine by emulsifying an aq. soln. of an antigen and a sulfolipid **polysaccharide**. The adjuvants are stable at high temps., and are at least as effective as convenient adjuvants. Their local toxicity is generally lower than that of conventional adjuvants. Thus, 6.6. g of lauroyl chloride was added to a soln. of 4.5 g inulin in 100 mL of DMF:pyridine (1:1), stirred and incubated for 6 h at 60.degree. and 18 h at room temp. followed by addn. of 0.6 g chlorosulfonic acid in 10 mL of DMF:pyridine and stirring and incubation at 60.degree. and room temp. was repeated. The solvents were then evapd. under reduced pressure and the sulfolipid **polysaccharide** thus obtained was dialyzed in phosphate buffered saline for 10 days, then **lyophilized**. An emulsion contg. 1, **Tween** 80 2, squalene 10, and phosphate

buffered saline q.s. 100% was stable after 115 days at 37.degree.. Guinea pig immunized with vaccines contg. inactivated influenza virus and above adjuvant showed significant elevated serum **antibody** as compared with the controls.

L11 ANSWER 22 OF 37 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1996:217300 CAPLUS
TITLE: Development of stable **lyophilized** monoclonal **antibody** formulations: Effect of excipients on stability.
AUTHOR(S): Bam, Narendra B.; Dal Monte, Paul R.; Duddu, Sarma P.
CORPORATE SOURCE: Pharmaceutical Development, SmithKline Beecham Pharmaceuticals, King of Prussia, PA, 19406, USA
SOURCE: Book of Abstracts, 211th ACS National Meeting, New Orleans, LA, March 24-28 (1996), BIOT-143. American Chemical Society: Washington, D. C. CODEN: 62PIAJ
DOCUMENT TYPE: Conference; Meeting Abstract
LANGUAGE: English
AB In the development of proteins for therapeutic use, long term aggregation and degrdn. is usually prevented by **lyophilization**. The proteins have been traditionally protected from the stresses of freezing and drying by addn. of excipients like **sugars**, polymers and **surfactants** to formulations. We present studies on the effect of **sugars** (**sucrose**, mannitol and **trehalose**) and **surfactants** (**Tween**) and polymers (PEG, Dextran and PVP) on the stabilization against aggregation of a monoclonal **antibody**. Our studies include FTIR spectroscopy, Calorimetry and traditional bioanal. techniques for protein characterization. Although monoclonal **antibodies** differ significantly in structure to commonly studied globular proteins, the stabilizing effect of **sugars** like **sucrose** and **trehalose** has been obsd. to be similar to that reported in literature. The importance of the relationship between the storage temp. of a lyophile and the glass transition temp. (Tg) will be stressed. We will also present data comparing and delineating whether the stabilization occurs during **lyophilization** or during reconstitution of the dried product.

L11 ANSWER 23 OF 37 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1995:576784 CAPLUS
DOCUMENT NUMBER: 122:299132
TITLE: Liposomes containing particulate materials
INVENTOR(S): Gregoriadis, Gregory; Antimisiaris, Sophia George; Gursel, Ihsan
PATENT ASSIGNEE(S): United Kingdom Secretary of State for Defence, London, UK
SOURCE: PCT Int. Appl., 35 pp. CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

WO 9509610	A1	19950413	WO 1994-GB2191	19941007
W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, ES, FI, GB, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LT, LU, LV, MD, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TJ, TT, UA, US, UZ, VN				
RW: KE, MW, SD, SZ, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2173601	AA	19950413	CA 1994-2173601	19941007
AU 9477907	A1	19950501	AU 1994-77907	19941007
AU 687893	B2	19980305		
EP 722317	A1	19960724	EP 1994-928490	19941007
EP 722317	B1	20011121		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, SE				
GB 2297907	A1	19960821	GB 1996-7359	19941007
GB 2297907	B2	19971210		
BR 9407769	A	19970318	BR 1994-7769	19941007
JP 09503225	T2	19970331	JP 1994-510702	19941007
CN 1200668	A	19981202	CN 1994-194325	19941007
RU 2145212	C1	20000210	RU 1996-110886	19941007
US 6322809	B1	20011127	US 1996-624556	19960920
PRIORITY APPLN. INFO.:			GB 1993-20668 A	19931007
			WO 1994-GB2191 W	19941007

AB A method is provided for the formation of liposomes of 0.1 .mu.m to 50 .mu.m in diam. having unilamellar or multilamellar structure and contg. water-insol. or undissolved particulate materials comprising (a) forming liposomes and removing substantially all of any org. solvent used in their prepn., (b) **freeze-drying** the liposomes so formed and then (c) rehydrating them in intimate admixt. with the particulate material. Preferred encapsulated materials are particulate materials, most preferably microorganisms, plant or animal cells or water-insol. structures having org. solvent-labile biochem. or immunol. activity, but any water-insol. particulate may be encapsulated using the method. For example, catalysts or drugs that are sparingly sol. may also be so incorporated such that slow release into the patient's body may be provided while release of **detergents** included in many liposome prepn. protocols may be avoided.

IT **99-20-7, Trehalose**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(manuf. of liposomes contg. particulate materials)

L11 ANSWER 24 OF 37 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1995:386367 CAPLUS
DOCUMENT NUMBER: 122:142605
TITLE: Method for preparing liposomes
INVENTOR(S): Hsu, Chung C.
PATENT ASSIGNEE(S): Genentech, Inc., USA
SOURCE: PCT Int. Appl., 26 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

WO 9501164		A1	19950112	WO 1994-US7327	19940629
	W: AU, CA, JP				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
CA 2163860		AA	19950112	CA 1994-2163860	19940629
AU 9472151		A1	19950124	AU 1994-72151	19940629
AU 689786		B2	19980409		
EP 706374		A1	19960417	EP 1995-904347	19940629
EP 706374		B1	19971210		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
JP 08512056		T2	19961217	JP 1994-503613	19940629
US 5653996		A	19970805	US 1995-407424	19950317
PRIORITY APPLN. INFO.:				US 1993-84933	19930630
				WO 1994-US7327	19940629

AB Methods are provided for the prepn. of liposomes by spraying a soln. comprising bilayer-forming matters, and optional addnl. mols. onto an aq. surface, through a frequency-generated vibrating nozzle without added pressure. The liposomes are useful for the delivery of therapeutic, diagnostic, and cosmetic agents. This method provides an economic and efficient method of prepg. liposomes on a large scale. For example, a soln. contg. dipalmitoylphosphatidylcholine, palmitoyloleoylphosphatidylglycerol, lung **surfactant** protein C, and palmitic acid in isopropanol was sprayed onto a succinate buffer soln. and the obtained liposome soln. was ultrafiltrated via tangential flow filtration and **lyophilized**.

L11 ANSWER 25 OF 37 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER:	1994:696634 CAPLUS
DOCUMENT NUMBER:	121:296634
TITLE:	**Lyophilized** ligand-receptor complexes for assays and sensors
INVENTOR(S):	Ligler, Frances S.; Whelan, James P.
PATENT ASSIGNEE(S):	United States Dept. of the Navy, USA; U.S. Drug Testing, Inc.
SOURCE:	U.S., 14 pp. CODEN: USXXAM
DOCUMENT TYPE:	Patent
LANGUAGE:	English
FAMILY ACC. NUM. COUNT:	1
PATENT INFORMATION:	

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5354654	A	19941011	US 1993-92518	19930716
WO 9502703	A1	19950126	WO 1994-US7806	19940715
W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, ES, FI, GB, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LT, LU, LV, MD, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TJ, TT, UA, UZ, VN				
RW: KE, MW, SD, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2167275	AA	19950126	CA 1994-2167275	19940715
AU 9473603	A1	19950213	AU 1994-73603	19940715
AU 685148	B2	19980115		
EP 710293	A1	19960508	EP 1994-922533	19940715

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE

PRIORITY APPLN. INFO.: US 1993-92518 19930716
WO 1994-US7806 19940715

AB A dry reagent prepd. by **lyophilizing** a labeled ligand-immobilized receptor complex or a labeled receptor-immobilized ligand complex is, on rehydration, useful for detecting analytes in samples in a variety of displacement assays. Prepn. of a **lyophilized** support and use of **lyophilized** beads in a flow immunosensor are described, as is a **lyophilization** ELISA plate assay.

IT **50-99-7, Glucose**, analysis
RL: ANT (Analyte); ANST (Analytical study)
(**lyophilized** ligand-receptor complexes for assays and sensors)

L11 ANSWER 26 OF 37 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1994:638436 CAPLUS
DOCUMENT NUMBER: 121:238436
TITLE: Synthetic particulate vectors comprising a non-liquid hydrophilic nucleus and amphiphilic outer layer
INVENTOR(S): Samain, Daniel; Delrieu, Pascal; Gibilaro, Joelle; Dirson, Roselyne; Cervilla, Monique; De Miguel, Ignacio; Ding, Li; Nguyen, Frederique; Soulet, Nadine; Soler, Corinne
PATENT ASSIGNEE(S): A et S Biovecteurs, Fr.
SOURCE: PCT Int. Appl., 45 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9420078	A1	19940915	WO 1994-FR228	19940301
W: CA, JP, KR, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
FR 2702160	A1	19940909	FR 1993-2397	19930302
FR 2702160	B1	19950602		
CA 2157384	AA	19940915	CA 1994-2157384	19940301
EP 687173	A1	19951220	EP 1994-908391	19940301
EP 687173	B1	19970917		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
JP 08507765	T2	19960820	JP 1994-519654	19940301
EP 782851	A1	19970709	EP 1997-102586	19940301
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
EP 787479	A1	19970806	EP 1997-104152	19940301
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
AT 158179	E	19971015	AT 1994-908391	19940301
ES 2108432	T3	19971216	ES 1994-908391	19940301
US 6013284	A	20000111	US 1996-513853	19960501

PRIORITY APPLN. INFO.: FR 1993-2397 19930302

EP 1994-908391 19940301
WO 1994-FR228 19940301

AB A synthetic particulate vector for pharmaceutical, cosmetic, or food prepns. comprises a non-liq. hydrophilic nucleus (e.g. a **polysaccharide**) and an outer layer at least partially consisting of amphiphilic compds. (e.g. phospholipids) and combined with the nucleus by hydrophobic interactions and/or ionic bonds. Amylopectin was mixed with 2N NaOH followed by addn. of a soln. of glycidyl trimethylammonium chloride in water and epichlorhydrine; the mixt. was then homogenized and the pH was set to 6 to obtain a gel which was washed and **lyophilized**. Thus, 0.6 g **glucose** oxidase (I) was mixed with 0.3 g above gel; the mixt. was then hydrated with 1.5 mL of buffer, pH = 7, and stirred at 4.degree. overnight and **lyophilized**. The above lyophilyzate was mixed with 0.15 g of hydrogenated soy phosphatidylcholine and 150 mL water, then it was homogenized to obtain I microcapsules with 92% microencapsulation.

L11 ANSWER 27 OF 37 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1994:517757 CAPLUS
DOCUMENT NUMBER: 121:117757
TITLE: Synthesis of polymer bioactive conjugates
INVENTOR(S): Marcucci, Fabrizio; Gregory, Ruth
PATENT ASSIGNEE(S): Farmitalia Carlo Erba S.R.L., Italy
SOURCE: PCT Int. Appl., 44 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9413322	A1	19940623	WO 1993-EP3429	19931206
W: AT, AU, BB, BG, BR, BY, CA, CH, CZ, DE, DK, ES, FI, GB, HU, JP, KP, KR, KZ, LK, LU, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SK, UA, US, VN				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2150925	AA	19940623	CA 1993-2150925	19931206
AU 9456968	A1	19940704	AU 1994-56968	19931206
AU 678796	B2	19970612		
EP 675736	A1	19951011	EP 1994-902692	19931206
EP 675736	B1	19980715		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
JP 08504202	T2	19960507	JP 1993-513763	19931206
AT 168273	E	19980815	AT 1994-902692	19931206
ES 2121180	T3	19981116	ES 1994-902692	19931206
US 6172202	B1	20010109	US 1997-889049	19970707

PRIORITY APPLN. INFO.: GB 1992-25448 A 19921204
WO 1993-EP3429 W 19931206

AB A process for the prepn. of a conjugate between a polymer and a first substance having a biol. activity mediated by a domain consists of (a) contacting the first substance with a second substance which specifically binds to the domain of the first substance, (b) conjugating a polymer to the first substance having the second substance bound and (c) freeing the second substance from

the first substance having the polymer conjugate. The advantages such as prolonged half-life in vivo and reduced immunogenicity in proteins, that can be derived from the conjugation of polymers to drugs or diagnostic reagents are maintained. Thus, a PEG_monoclonal **antibody** conjugates (**mAb** 78) **lyophilized** formulation was prepd. contg. drug 0.05-0.5, excipient such as **lactose** or mannitol 2.5-5.0, **surfactant** (e.g., Poloxamer) 0.0025-0.025% (wt./vol.) and 6.5-7 pH-adjusting agent. The conjugate displayed a better retention of biol. activity than the unprotected conjugates.

L11 ANSWER 28 OF 37 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1994:491424 CAPLUS
DOCUMENT NUMBER: 121:91424
TITLE: Removal/neutralization of hepatitis A virus during manufacture of high purity, solvent/**detergent** factor VIII concentrate
AUTHOR(S): Lemon, Stanley M.; Murphy, Paula C.; Smith, Andrew; Zou, Jinsheng; Hammon, John; Robinson, Stephen; Horowitz, Bernard
CORPORATE SOURCE: Dep. Med., Univ. North Carolina, Chapel Hill, NC, USA
SOURCE: J. Med. Virol. (1994), 43(1), 44-9
CODEN: JMVIDB; ISSN: 0146-6615
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Recent reports have suggested an increased risk of type A viral hepatitis in hemophilic patients treated with high purity factor VIII concs. prepd. using ion exchange chromatog. coupled with solvent/**detergent** treatment for inactivation of viruses. To det. the capacity for removal or inactivation of hepatitis A virus during the factor VIII manufg. process, human plasma and various factor VIII prodn. intermediates were spiked with cell culture-propagated virus and subjected to scaled down conditions mimicking the manuf. of solvent/**detergent** factor VIII. The combination of **antibody**-mediated neutralization, cryopptn., anion exchange chromatog., and **lyophilization** in the absence of **sucrose** resulted in a minimal redn. of 5.5 to 8.55 log10 in the infectivity of hepatitis A virus.

L11 ANSWER 29 OF 37 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1991:160306 CAPLUS
DOCUMENT NUMBER: 114:160306
TITLE: Immunoassay **lyophilized** reactant mixture
INVENTOR(S): Cole, Francis X.
PATENT ASSIGNEE(S): Hygeia Sciences, Inc., USA
SOURCE: PCT Int. Appl., 32 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9013637	A1	19901115	WO 1990-US2064	19900416
W: CA, JP				

RW: AT, BE, CH, DE, DK, ES, FR, GB, IT, LU, NL, SE					
US 5102788	A	19920407	US 1989-344575	19890428
CA 2053885	AA	19901029	CA 1990-2053885	19900416
EP 470192	A1	19920212	EP 1990-908003	19900416
EP 470192	B1	19971008		
R: AT, BE, CH, DE, DK, ES, FR, GB, IT, LI, LU, NL, SE				
JP 05500854	T2	19930218	JP 1990-506814	19900416
AT 159047	E	19971015	AT 1990-908003	19900416
ES 2110415	T3	19980216	ES 1990-908003	19900416
PRIORITY APPLN. INFO.:			US 1989-344575	19890428
			US 1985-747605	19850624
			US 1988-275656	19881121
			WO 1990-US2064	19900416

AB A **lyophilized** mixt. of reactants for an immunoassay includes **antibody**-gold sol particle conjugates, **antibody** latex particle conjugates, polyethylene glycol, a polyethylene glycol p-isooctylphenyl ether **detergent** and dextrin or **trehalose**. The polyethylene glycol is present to enhance binding of the immunoreactants and the polyethylene glycol p-isooctylphenyl ether **detergent** is present to prevent nonspecific interactions. The dextrin or threhalose prevents agglomeration of the polyethylene glycol and polyethylene glycol p-isooctylphenyl ether in the **lyophilized** mixt. at room temp. and facilitates retention of homogenous distribution of the ingredients of the mixt. to thereby enhance shelf life and redistribution of the mixt. in an aq. test system. Thus, an aq. mixt. to be subjected to **lyophilization** contained anti-human chorionic gonadotropin **antibody** conjugated to Au sol particles, a 2nd anti-human chorionic gonadotropin **antibody** conjugated to carboxylated modified latex particles, polyethylene glycol, Thimoseral, Tris buffer, Maltrin, disodium EDTA, and IGEPAl CA720.

IT **99-20-7, Trehalose**
RL: ANST (Analytical study)
(in immunoassay **lyophilized** reagent mixt. as antiagglomerant)

L11 ANSWER 30 OF 37 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER:	1990:527184 CAPLUS
DOCUMENT NUMBER:	113:127184
TITLE:	Enzyme immunoassays and immunologic reagents for home diagnostic application
INVENTOR(S):	Block, Elliott; Bahar, Izak; Cole, Frank; Eaton, Cheryl A.; Jones, Wendy; Sigillo, Eric; Coseo, Mary; Cicia, Nancy J.; Cannon, L. Edward; Cantarow, Walter
PATENT ASSIGNEE(S):	Hygeia Sciences, Inc., USA
SOURCE:	U.S., 15 pp. Cont. of U.S. Ser. No. 747,605, abandoned. CODEN: USXXAM
DOCUMENT TYPE:	Patent
LANGUAGE:	English
FAMILY ACC. NUM. COUNT:	2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 4931385	A	19900605	US 1988-275656	19881121

US 5102788 A 19920407 US 1989-344575 19890428
PRIORITY APPLN. INFO.: US 1983-473907 19830310
US 1985-747605 19850624
US 1988-275656 19881121

AB Enzyme immunoassays, esp. ELISAs, for home diagnostic application under ambient room temp. and humidity, use a **lyophilized** mixt. contg. peroxidase-**antibody** conjugate, a binding-enhancer (e.g. PEG, polyvinyl alc., polyvinyl pyrrolidone, and dextran), a water-sol. nonionic **surfactant** in an amt. sufficient to provide detergency without having a deleterious effect on the conjugate, and a **sugar** (dextrin or **trehalose**). For an ELISA, a solid support is precoated with another **antibody** and then is treated with a blocking soln. comprising a blocking agent (bovine serum albumin, gelatin, milk proteins, or nonspecific IgG) and a water-sol. **sugar**. Both the **lyophilized antibody** conjugate mixt. and the immobilized **antibody** have preserved reactivity and immunolysis binding specificity even if exposed to high humidity and temps. of 80-120.degree.F prior to their use in the immunoassay. A diagnostic kit for the ELISA is disclosed. An ELISA for human chorionic gonadotropin (hCG) in urine used (1) **lyophilized** mixt. contg. peroxidase conjugated with a monoclonal **antibody** to the .beta.-chain of hCG, PEG, Hepes salt, Hepes acid, di-Na EDTA, $MgSO_4$, dextrin, and IGEPAL CA-630 (octylphenoxypoly(ethyleneoxy)ethanol); (2) dipsticks coated with monoclonal **antibody** to hCG and treated with bovine serum albumin and **sucrose** in the blocking soln.; and (3) a chromogen soln. contg. tetramethylbenzidine, buffer, and H_2O_2. Urine was added to the conjugate mixt. and the dipstick was immersed in the soln. for >15 min. The dipstick was removed, washed with tap water, and dipped in the chromogen soln. for >5 min. When hCG was present, the dipstick changed from colorless to blue-green.

IT **57-50-1, Sucrose**, biological studies
RL: BIOL (Biological study)
(blocking soln. contg. bovine serum albumin and, for stable **antibody**-coated dipstick for home diagnostic ELISA)

IT **99-20-7, Trehalose**
RL: BIOL (Biological study)
(heat- and humidity-stable **lyophilized** mixt. contg. peroxidase-**antibody** conjugate and, for home diagnostic ELISA)

L11 ANSWER 31 OF 37 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1989:436239 CAPLUS
DOCUMENT NUMBER: 111:36239
TITLE: Device and method for biochemical assay
INVENTOR(S): Stanley, Christopher John; Johannsson, Axel
PATENT ASSIGNEE(S): IQ (BIO) Ltd., UK
SOURCE: PCT Int. Appl., 49 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 8804428	A1	19880616	WO 1987-GB899	19871211

W: AU, DK, JP, US
RW: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE

AU 8783339	A1	19880630	AU 1987-83339	19871211
DK 8804488	A	19880811	DK 1988-4488	19880811
PRIORITY APPLN. INFO.:			GB 1986-29740	19861212
			WO 1987-GB899	19871211

AB An app. for carrying out a biochem. assay, e.g. an immunoassay or nucleic acid hybridization assay, comprises a hard polystyrene reaction surface adapted to bind a 1st biochem. ligand (e.g. a monoclonal **antibody**), a liq. absorbent wadding adjacent to the reaction surface to absorb washing soln. applied to the reaction surface, a filter matrix overlying the reaction surface in close contact therewith for filtering a sample and for retaining a 2nd biochem. ligand in contact with the reaction surface, wherein the 2nd ligand can specifically bind to the 1st ligand on the surface. The filter matrix is removable to facilitate washing of the reaction surface, and the filter matrix comprises a labeled substance capable of a specific binding reaction at the reaction surface during the assay. Polystyrene strips (for reaction surfaces) were dipped into monoclonal anti-Chlamydia **antibody** (5 .mu.g/mL) and incubated overnight at 37.degree. before dipping in glazing soln. (**lactose**, degraded gelatin, thimerosal, and **Tween** 20) and air drying. Latex-filled paper (filter matrix) was preblocked by immersion for 1 h in the glazing soln., and a soln. contg. Fab' fragments of anti-Chlamydia **antibody** conjugated to alk. phosphatase was pipetted onto 10-mm2 paper squares. The conjugate was **freeze-dried** into the filter matrix. A liq. sample contg. Chlamydia antigen was applied to the filter matrix on the polystyrene reaction surface, the reaction surface was washed with buffer contg. diethanolamine, iodonitrotetrazoleum violet, NaN3, EDTA, and EtOH, and developed using a developer pad contg. Cu-activated pig heart diaphorase, alc. dehydrogenase, **sucrose**, Triton X-705, gelatin, and Tris. A red color appeared on the developer pad within 5 min.

L11 ANSWER 32 OF 37 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER:	1989:73606 CAPLUS
DOCUMENT NUMBER:	110:73606
TITLE:	Cytotoxic liposomes: membrane interleukin 1 presented in multilamellar vesicles
AUTHOR(S):	Bakouche, Ouahid; Lachman, Lawrence B.; Knowles, Rebecca D.; Kleinerman, Eugenie S.
CORPORATE SOURCE:	Dep. Cell Biol., M. D. Anderson Hosp., Houston, TX, 77030, USA
SOURCE:	Lymphokine Res. (1988), 7(4), 445-56 CODEN: LYREDH; ISSN: 0277-6766
DOCUMENT TYPE:	Journal
LANGUAGE:	English

AB Paraformaldehyde-fixed **lipopolysaccharide** (LPS)-activated human monocytes produced significant lysis of the human melanoma cell line A375. The cytotoxic activity was retained following treatment of the fixed monocytes with anti-tumor necrosis factor (anti-TNF) **antibodies** but was specifically inhibited by a mixt. of anti-TNF and anti-interleukin 1 (anti-IL-1) **antibodies**. A375 cells were also killed by plasma membranes purified from LPS-activated human blood monocytes. This activity was specifically inhibited by anti-IL-1 .alpha. **antibodies** , but only partially inhibited by anti-IL-1 .beta.

antibodies. CHAPS **detergent**-extd. plasma-membrane IL-1 in its sol. form or assocd. with **lyophilized** liposomes was also able to kill A375 cells, and this antitumor activity was inhibited by anti-IL-1 **antibodies**. These results suggest that membrane IL-1, primarily IL-1 .alpha., was cytotoxic for the A375 cells. CKS-17, a peptide synthesized with homol. to a highly conserved region of the immunosuppressive retroviral envelope protein P15E, when covalently bound to BSA, partially inhibited the IL 1 activities of tumor cell cytotoxicity and T-cell clone proliferation, displayed by purified plasma membranes, **detergent**-extd. membrane IL 1, or membrane IL 1 assocd. with liposomes. Thus, cytotoxic membrane IL-1 can be solubilized by **detergent**, bound to the surface of liposomes, and specifically inhibited by anti-IL-1 **antibodies** or the immunosuppressive peptide CKS-17.

L11 ANSWER 33 OF 37 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1988:545719 CAPLUS
DOCUMENT NUMBER: 109:145719
TITLE: Enzyme immunoassay-monoclonal test system for the detection of plague pathogens
AUTHOR(S): Temiralieva, G. A.; Arakelyan, I. S.; Lukhnova, L. Yu.; Apsatarova, R. A.
CORPORATE SOURCE: Sredneaziat. Nauchno-Issled. Protivochumn. Inst., Alma-Ata, USSR
SOURCE: Lab. Delo (1988), (8), 61-3
CODEN: LABDAZ; ISSN: 0023-6748
DOCUMENT TYPE: Journal
LANGUAGE: Russian
AB EIA based on the use of monoclonal **antibodies** (isolated from ascitic fluid), described for detecting plague pathogen under lab. and field conditions, uses **antibody**-horseradish peroxidase conjugates and **Tween** as the reaction stabilizer. The conjugates were prepd. by periodate method. Caprylic acid gave the most pure plague monoclonal Igs, the diln. of the conjugates was .gtoreq.1:1000. One part Ig and 2 parts of the enzyme was the best ratio. This conjugate ratio can detect 30 ng/mL plague microbes. Medium contg. polyvinylpyrrolidone with 7.5% **sucrose** was the best for **lyophilizing** the conjugates. The **lyophilized** conjugates preserved their sp. activity for 2 yr at -20.degree. to 25.degree.. The EIA had higher sensitivity than the agglutination test.

L11 ANSWER 34 OF 37 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1986:107939 CAPLUS
DOCUMENT NUMBER: 104:107939
TITLE: Preparation of pure yeast chromatin
INVENTOR(S): Shalitin, Channa
PATENT ASSIGNEE(S): Technion Research and Development Foundation Ltd., Israel
SOURCE: Ger. Offen., 27 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

DE 3525722	A1	19860123	DE 1985-3525722	19850718
IL 72452	A1	19880429	IL 1984-72452	19840719
IL 82930	A1	19880429	IL 1984-82930	19840719
CA 1279589	A1	19910129	CA 1985-485680	19850627
ZA 8505012	A	19860226	ZA 1985-5012	19850703
GB 2163165	A1	19860219	GB 1985-17078	19850705
GB 2163165	B2	19880720		

PRIORITY APPLN. INFO.: IL 1984-72452 19840719

AB Yeast chromatin is purified by d. gradient centrifugation of the cell homogenate. Thus, baker's yeast cells were disrupted with glass beads. Phenylmethylsulfonyl fluoride (I) was added and the mixt. centrifuged. The chromatin pellet was suspended in pH 7.5 buffer contg. I, a **surfactant**, and an antioxidant and centrifuged. The pellet was suspended and centrifuged through a **sucrose** soln. Purified chromatin was treated with a nuclease in buffer contg. I and centrifuged. The supernatant was centrifuged on a 5-20% **sucrose** gradient and sep. fractions were dialyzed and **lyophilized** to obtain p20 protein. The p20 protein may be injected, with an adjuvant, into lab animals to elicit the formation of **antibodies** to ras oncogene proteins.

IT **57-50-1**, biological studies
RL: BIOL (Biological study)
(in chromatin purifn., from yeast)

L11 ANSWER 35 OF 37 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1984:412196 CAPLUS
DOCUMENT NUMBER: 101:12196
TITLE: Gamma globulin-containing compositions
INVENTOR(S): Hooper, John A.; Mankarious, Samia; Liu-Rash, Catherine R.
PATENT ASSIGNEE(S): Baxter Travenol Laboratories, Inc., USA
SOURCE: PCT Int. Appl., 21 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 8400891	A1	19840315	WO 1983-US1016	19830701
W: JP				
RW: AT, BE, CH, DE, FR, GB, SE				
EP 116571	A1	19840829	EP 1983-902407	19830701
EP 116571	B1	19910828		
EP 116571	B2	19971029		
R: AT, BE, CH, DE, FR, GB, LI, SE				
JP 59501546	T2	19840830	JP 1983-502448	19830701
JP 08000787	B4	19960110		
AT 66616	E	19910915	AT 1983-902407	19830701
CA 1239584	A1	19880726	CA 1983-433121	19830725
ES 524890	A1	19860201	ES 1983-524890	19830811

PRIORITY APPLN. INFO.: US 1982-413059 19820830
EP 1983-902407 19830701
WO 1983-US1016 19830701

AB The anticomplement activity of .gamma.-globulin products prepd. by

methods involving ultrafiltration and(or) treatment with ion exchangers is considerably decreased by including .gtoreq.1 non-**surface-active** stabilizers such as hydrophilic macromols., amino acids, and low mol. wt. polyols with .gamma.-globulin concns. during ultrafiltration and(or) ion exchange. An aq. soln. of Cohn Fraction II at a protein concn. of 50 g/L and pH 5.3 was dialyzed against 4 vols. of a soln. contg. 20 mM NaCl and 0.5 g/L PEG-4000 [25322-68-3]. The Fraction II soln. was pumped through Millipore cassettes where materials with mol. wt. of <100,000 Daltons were removed by ultrafiltration. The retentate which contained concd. Ig was returned to and mixed with Ig soln. undergoing dialysis. The dialysis soln. was continuously pumped into the Ig soln. at the same rate as filtrate was produced and removed. When 300 L dialysis soln. was depleted, the Ig soln. was concd. to a protein concn. of 55 mg/mL, and the concd. Ig soln. treated with hydrated DEAE Sephadex A-50 (5 g/g protein), agitated for 3 h at 5.degree., and filtered. NaCl, dextrose [**50-99-7**], glycine [56-40-6], and albumin were added to the soln. to a final concn. of 0.85, 2.0, 2.25, and 0.1%, resp., the pH adjusted to 7.0 and protein concn. adjusted to 5.2%. The soln. contained .apprx.1.3 mg PEG-4000/mL from the dialysis step. The soln. was sterile filtered, filled into vials, **lyophilized** and the vial sealed.

IT **50-99-7**, biological studies
RL: BIOL (Biological study)
(anticomplement activity of .gamma.-globulin concs. decreased by)

L11 ANSWER 36 OF 37 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1971:417780 CAPLUS
DOCUMENT NUMBER: 75:17780
TITLE: Possibility of producing antigens from Histoplasma capsulatum using **detergents**
AUTHOR(S): Cherepanov, N. M.; Lipnitskii, A. V.; Borod'ko, S. L.
CORPORATE SOURCE: Rostov. Nauchno-Issled. Protiv. Inst., Rostov-on-Don, USSR
SOURCE: Sb. Nauch. Rab., Volgograd. Gos. Med. Inst. (1969), 22, 512-14
CODEN: SNVMBP
DOCUMENT TYPE: Journal
LANGUAGE: Russian

AB Antigens were extd. from **freeze-dried** mycelium of H. capsulatum with cetyltrimethylammonium bromide (I), Na glycocholate (II), Na oleate (III), sulfanol (IV), and **Tween** 80 (V). Obtained antigenic fractions were mainly **polysaccharide** and had a low nucleic acid content (0.1-0.4%). The protein content depended on the type of **detergent** used in the extn. procedure. Antigens extd. with I, II, III, IV, and V contained 17.5, 20, 36.2, 42.5, and 24% protein resp. For immunol. characterization the antigenic activity of fractions was compared with that of the antigen obtained by the conventional .beta.-naphthol method. According to passive hemagglutination and **antibody** neutralization reactions, antigen fractions obtained by extn. with IV and I were at least as active as that prepd. by the .beta.-naphthol method. A lower antigen content was found in fractions obtained by extn. with II, III, and esp. with V. All fractions showed 2 pptg. zones in gel with serums of hyperimmunized rabbits. Antigen extn. with the